Urological infection

Define the common terms used to describe GU infections?

1) UTI
    - **inflammatory response of urothelium to bacterial invasion** that is usually associated with bacteriuria and pyuria
2) bacteriuria
    - **Bacteria in urine** (normally free of bacteria)
    - bacteria may be
        - i. in urothelium without bacteriuria and alternatively,
        - ii. bacteriuria may represent bacterial contamination of a sterile specimen
    - ***S/P aspiration is most reliable specimen***, then catheterized, then voided
    - symptomatic vs asymptomatic bacteriuria
3) pyuria
    - **WBCs in the urine** (generally indicative of infection & inflammatory response of the urothelium to bacterium)
    - ***bacteriuria w/o pyuria***
        - o indicates colonization without infection
    - ***pyuria w/o bacteruiria (sterile pyuria)***
        - o ***may indicate TB, stones, cancer, etc***
4) cystitis
    - **Clinical syndrome** of dysuria, frequency, urgency, and occasionally S/P pain
    - may be associated with infection of urethra, vagina, or other noninfectious conditions such as IC, bladder carcinoma, or stones

5) acute pyelonephritits
    - ***clinical syndrome*** of **fever, chills, and flank pain** accompanied by **bacteriuria and pyuria**
    - difficult to diagnose in patients with SCI and the elderly

6) chronic pyelo
    - describes a **shrunken, scarred kidney**, **post-infectious** (frequently not associated with UTI)
    - may cause ***focal, coarse scar in renal cortex overlying a calyx***, and usually ***calyceal distortion***.
    - less commonly, renal scarring from infection → atrophic pyelonephritis or generalized thinning of the renal cortex

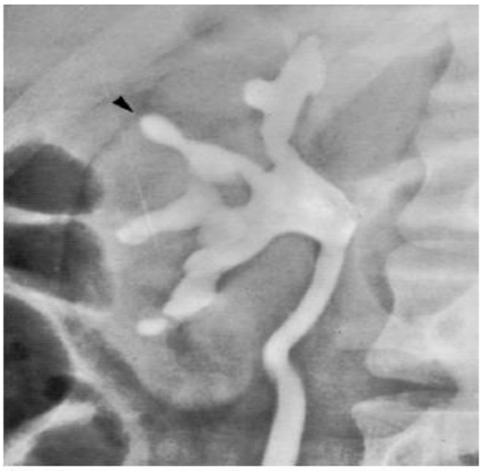


Figure 10–1. Excretory urogram demonstrates focal, coarse scarring in the right kidney of an 18-year-old girl with a history of many recurrent fevers between 2 months and 2 years of age. A cystogram when the patient was 2 years old established an atrophic left kidney with marked reflux up to the left kidney and slight reflux up to the right kidney. Excretory urography at the age of 6 years established severe atrophy of the left kidney. She had no infections between the ages of 6 and 15 years. Several reinfections occurred at the age of 15 years, and they ceased with prophylactic therapy. Her blood pressure has remained normal, and her serum creatinine level was 0.9 mg/dL at the age of 18 years. At 21 years of age she stopped antimicrobial prophylaxis for 18 months without infections or introital colonization with Enterobacteriaceae. Note that all calyces are blunted and that one extends to the capsule *(arrowhead)* because of atrophy of the overlying cortex.

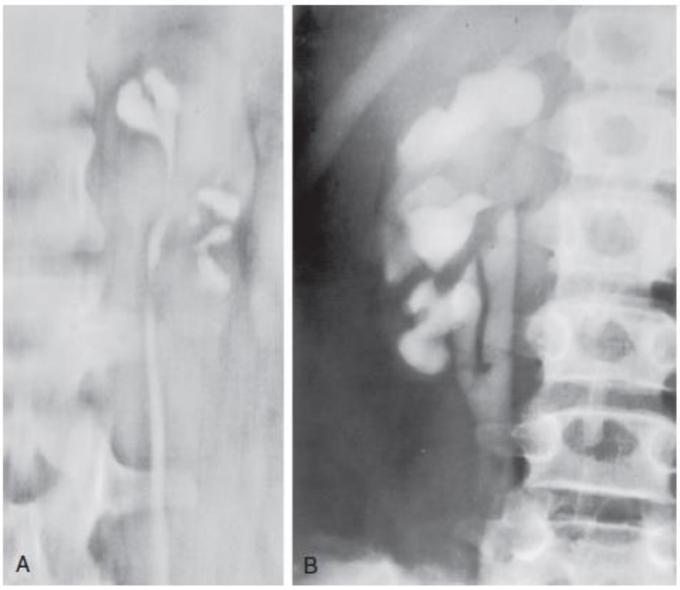
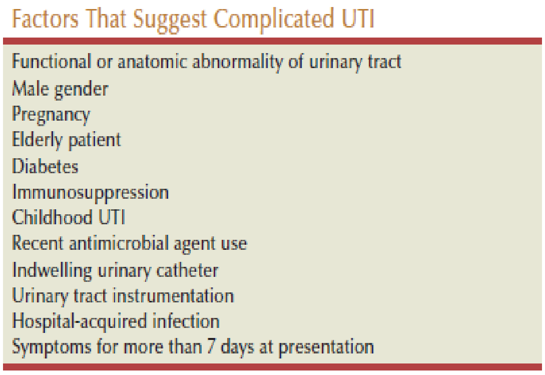


Figure 10–2. **A,** Excretory urogram of the contralateral left kidney from the same patient as in Figure 10–1. The severe pyelonephritic atrophy, undoubtedly caused by febrile urinary infections during early infancy with reflux into different segments of the kidney, produced irregular cortical scarring. Note how all the calyces extend to the capsule with irregular, intervening areas of cortex. **B,** Pyelonephritic atrophy, suggestive of postobstructive atrophy, in a 20-year-old woman with spina bifida, neurogenic bladder, and many episodes of fever and bacteriuria in early childhood. Observe the uniform, regular atrophy of the renal cortex that suggests reflux of bacteria simultaneously into virtually all nephrons. This type of pyelonephritic atrophy is uncommon compared with that shown in **A** and is characteristic of obstruction with superimposed infection.

7) uncomplicated UTI
   - Infection in a healthy pt. (structurally & functionally normal)
   - easily eradicated
   - no association with renal scarring, HTN, or ESRD

8) complicated UTI
   - The urinary tract is structurally or functionally abnormal, the host is compromised, and/or the bacteria have increased virulence or antimicrobial resistance.
   - Can lead to renal scarring, HTN, or ESRD



Factors That Suggest Complicated UTI

Functional or anatomic abnormality of urinary tract
Male gender
Pregnancy
Elderly patient
Diabetes
Immunosuppression
Childhood UTI
Recent antimicrobial agent use
Indwelling urinary catheter
Urinary tract instrumentation
Hospital-acquired infection
Symptoms for more than 7 days at presentation

9) First or isolated infection
   - patient *never had a UTI* or has *one remote from previous*

10) Unresolved UTI
   - has *not responded to ABx*

11) Recurrent UTI
   - after *resolution of an antecedent infection*

12) Reinfection
   - new event, *reintroduction* of bacteria from *outside GU tract*.

13) Bacterial persistence/relapse
   - recurrent UTI from same bacteria reemerging from a focus within the GU tract (eg stone)

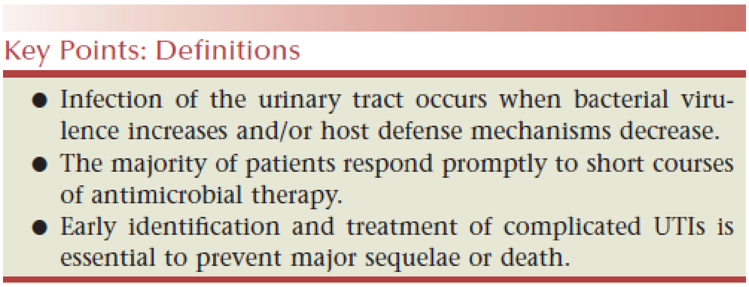
N.B:

- **Once a patient has an infection, he or she is likely to develop subsequent infections.**

- **Most reinfections occurred after 2 weeks.**
- **if antimicrobial prophylaxis is started after the second or any succeeding infection within a set, about two thirds of the women will benefit.**
- **Whether a patient receives no treatment at all or short-term, long-term, or prophylactic antimicrobial treatment the risk of recurrent bacteriuria remains the same; prophylactic antimicrobial therapy reduces reinfections but does not alter the underlying predisposition to recurring infection**

14) Prophylactic antimicrobial therapy
    - prevention of reinfection of urinary tract by the use of ABx

15) Suppressive antimicrobial therapy
    - suppression of focus of bacterial persistence can’t be eradicated.



Key Points: Definitions

- Infection of the urinary tract occurs when bacterial virulence increases and/or host defense mechanisms decrease.
- The majority of patients respond promptly to short courses of antimicrobial therapy.
- Early identification and treatment of complicated UTIs is essential to prevent major sequelae or death.

Different Classifications for UTI:

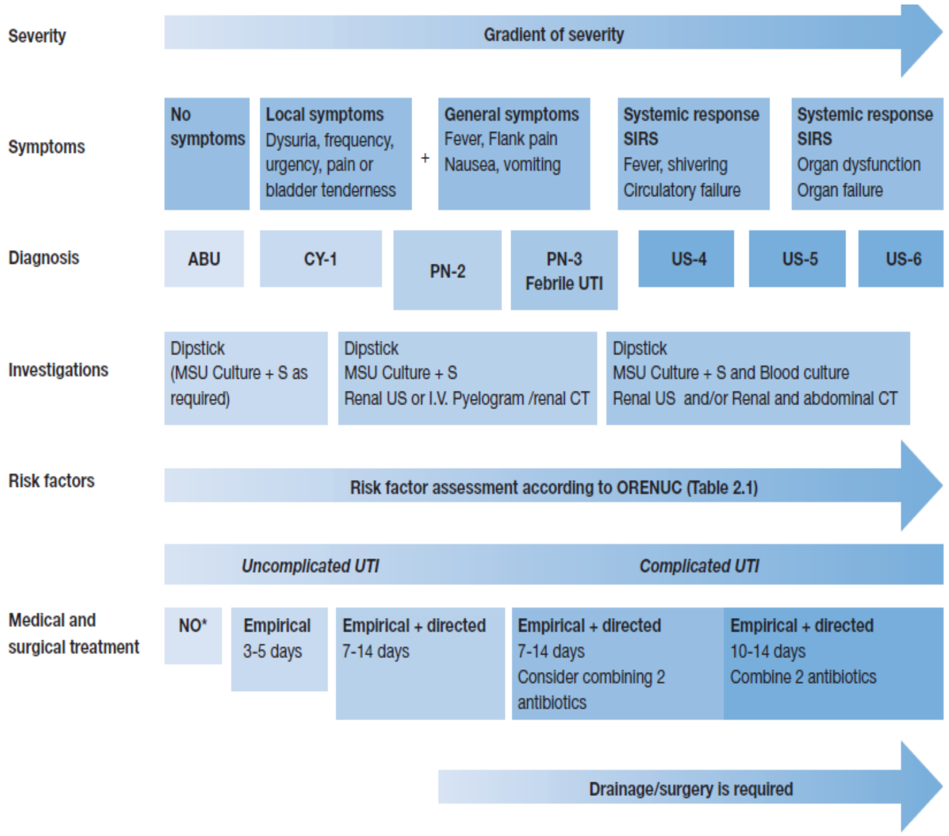
- Based on clinical symptoms, laboratory data, and microbiological findings.
- Tentative improved system of classification of UTI based on:
    - anatomical level of infection;
    - grade of severity of infection;
    - underlying risk factors;
    - microbiological findings.

1. Anatomical level of infection

- The symptoms, focus on anatomical level of infection, defined as:
  - urethra: urethritis (UR);
  - urinary bladder: cystitis (CY);
  - kidney: pyelonephritis (PN);
  - blood stream: sepsis (US).
- Asymptomatic bacteriuria (ABU)
  - have its source in both the lower and upper urinary tracts,
  - requires no treatment unless the patient is subjected to urological surgery.

2. Grade of severity

The grade of severity is set on a scale of 1-6 that is related to the risk of fatal outcome



Severity
Gradient of severity

Symptoms
No symptoms
Local symptoms Dysuria, frequency, urgency, pain or bladder tenderness
+
General symptoms Fever, Flank pain Nausea, vomiting
Systemic response SIRS Fever, shivering Circulatory failure
Systemic response SIRS Organ dysfunction Organ failure

Diagnosis
ABU
CY-1
PN-2
PN-3 Febrile UTI
US-4
US-5
US-6

Investigations
Dipstick (MSU Culture + S as required)
Dipstick MSU Culture + S Renal US or I.V. Pyelogram /renal CT
Dipstick MSU Culture + S and Blood culture Renal US and/or Renal and abdominal CT

Risk factors
Risk factor assessment according to ORENUC (Table 2.1)

Uncomplicated UTI
Complicated UTI

Medical and surgical treatment
NO*
Empirical 3-5 days
Empirical + directed 7-14 days
Empirical + directed 7-14 days Consider combining 2 antibiotics
Empirical + directed 10-14 days Combine 2 antibiotics

Drainage/surgery is required

3. Host risk factors:

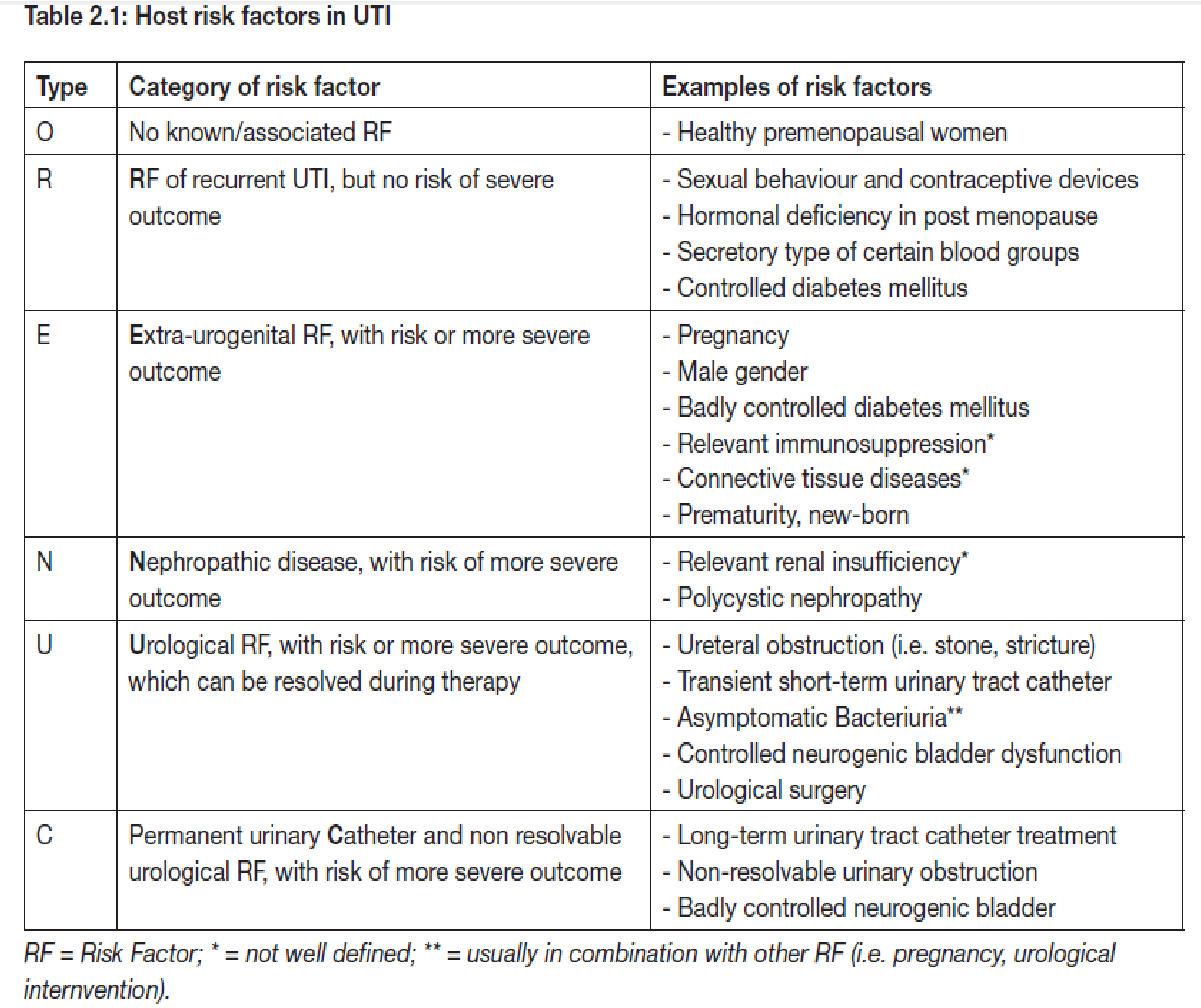


Table 2.1: Host risk factors in UTI

Type	Category of risk factor	Examples of risk factors
O	No known/associated RF	- Healthy premenopausal women
R	**R**F of recurrent UTI, but no risk of severe outcome	- Sexual behaviour and contraceptive devices - Hormonal deficiency in post menopause - Secretory type of certain blood groups - Controlled diabetes mellitus
E	**E**xtra-urogenital RF, with risk or more severe outcome	- Pregnancy - Male gender - Badly controlled diabetes mellitus - Relevant immunosuppression* - Connective tissue diseases* - Prematurity, new-born
N	**N**ephropathic disease, with risk of more severe outcome	- Relevant renal insufficiency* - Polycystic nephropathy
U	**U**rological RF, with risk or more severe outcome, which can be resolved during therapy	- Ureteral obstruction (i.e. stone, stricture) - Transient short-term urinary tract catheter - Asymptomatic Bacteriuria** - Controlled neurogenic bladder dysfunction - Urological surgery
C	Permanent urinary **C**atheter and non resolvable urological RF, with risk of more severe outcome	- Long-term urinary tract catheter treatment - Non-resolvable urinary obstruction - Badly controlled neurogenic bladder

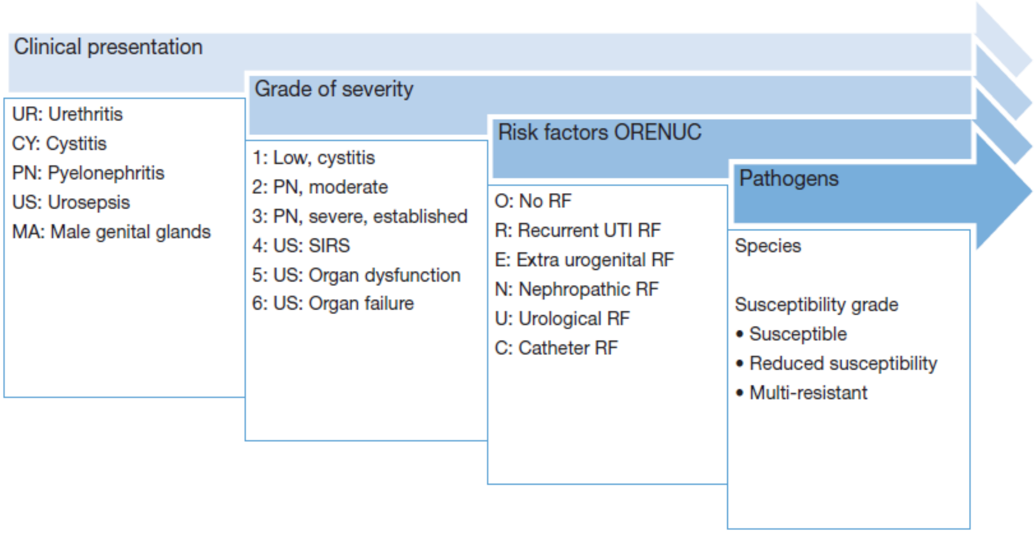
*RF = Risk Factor; * = not well defined; ** = usually in combination with other RF (i.e. pregnancy, urological internvention).*

4. Pathogens

- Urine culture will usually identify the causative pathogen ($\geq 10^4$ cfu/mL) and its susceptibility pattern.
- Both characteristics can be introduced in the final classification of the clinical stage of infection. The degree of susceptibility is defined as grade a (susceptible) to c (resistant).

Classification of UTI

A summary of the additive parameters that make up an individual class of UTI



By cumulating the different parameters, a UTI can be classified into:

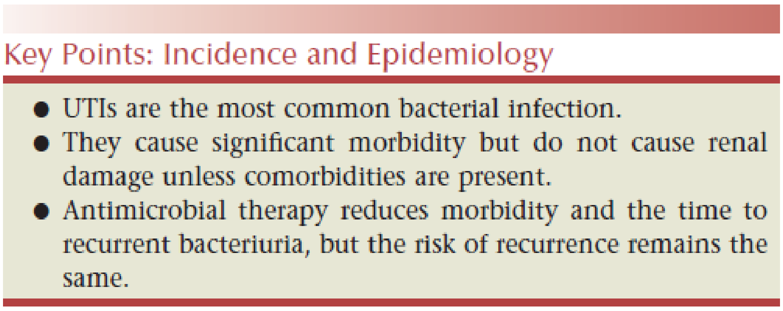
- **CY-1R:** *E. coli* (a): simple cystitis but recurrent with susceptibility to standard antibiotics.

- **PN-3U:** *K pneumonia* (b): severe pyelonephritis (with high fever and vomiting), with underlying urological disease (e.g. stones or obstruction) due to *Klebsiella* sp., with a moderate antibiotic resistance profile.

- **US-5C:** *Enterococcus* sp. (a): severe urosepsis with an antibiotic-sensitive *Enterococcus* sp. in a patient with an indwelling catheter.

INCIDENCE AND EPIDEMIOLOGY

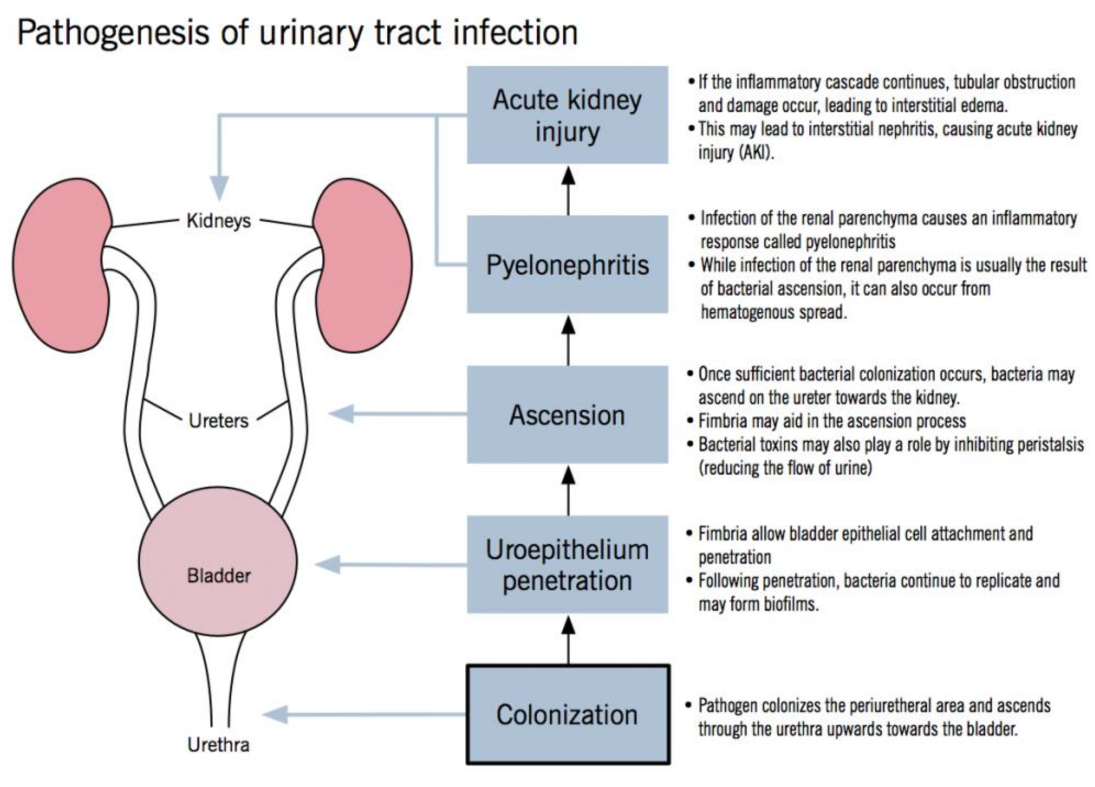
- Urinary tract infections (UTIs) are the most common bacterial infection (1.2% of F office visits, 0.6% M visits).
- UTIs → 40% of nosocomial infections (mostly catheter associated)
- **prevalence much higher in F**
- nearly 30% of F have symptomatic UTI by age 25, almost 50% during their lifetime



Key Points: Incidence and Epidemiology

- UTIs are the most common bacterial infection.
- They cause significant morbidity but do not cause renal damage unless comorbidities are present.
- Antimicrobial therapy reduces morbidity and the time to recurrent bacteriuria, but the risk of recurrence remains the same.

Pathogenesis of UTIs



- If the inflammatory cascade continues, tubular obstruction and damage occur, leading to interstitial edema.
- This may lead to interstitial nephritis, causing acute kidney injury (AKI).

- Infection of the renal parenchyma causes an inflammatory response called pyelonephritis
- While infection of the renal parenchyma is usually the result of bacterial ascension, it can also occur from hematogenous spread.

- Once sufficient bacterial colonization occurs, bacteria may ascend on the ureter towards the kidney.
- Fimbria may aid in the ascension process
- Bacterial toxins may also play a role by inhibiting peristalsis (reducing the flow of urine)

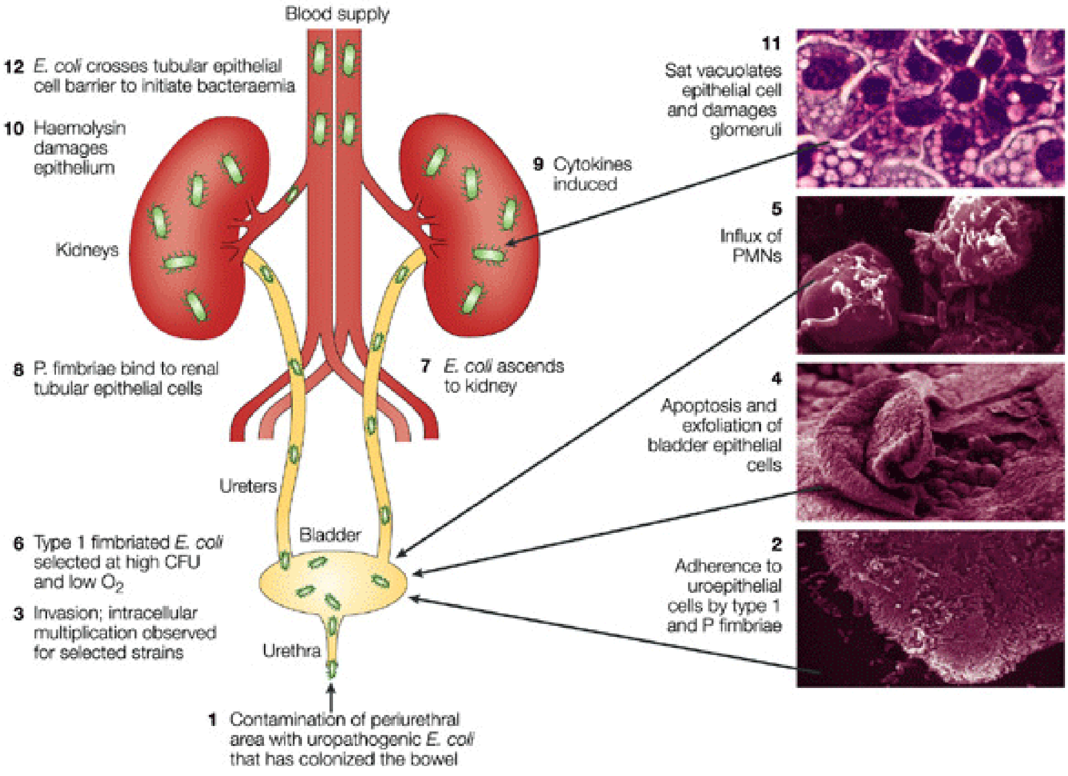
- Fimbria allow bladder epithelial cell attachment and penetration
- Following penetration, bacteria continue to replicate and may form biofilms.

- Pathogen colonizes the periurethral area and ascends through the urethra upwards towards the bladder.

Route:

- **Direct (Ascending)**:
  - from the **urethra** (**most common**) esp. enteric origin (e.g. *E. coli*). This explains:
    - women > men,
    - increased risk after bladder cath. or instrumentation.

  - Most episodes of pyelonephritis caused by **retrograde ascent** of bacteria from the bladder → ureter → renal pelvis and parenchyma
  - ***Reflux of urine is not required*** for ascending infections, but edema associated with cystitis may cause changes in the UVJ to permit reflux.
- haematogenous
  - few uncommon microbes, as *Staph. aureus*, *Candida* sp., *Salmonella* sp. and *Mycobacterium tuberculosis*.
  - Candida albicans: both haematogenous and direct infection → if catheter or after antibiotic therapy.
- lymphatic spread,
  - Direct extension of bacteria from the adjacent organs via lymphatics. In unusual circumstances, as a severe bowel infection or retroperitoneal abscesses.


Blood supply
12 E. coli crosses tubular epithelial cell barrier to initiate bacteraemia
10 Haemolysin damages epithelium
Kidneys
8 P. fimbriae bind to renal tubular epithelial cells
Ureters
6 Type 1 fimbriated E. coli selected at high CFU and low O2
3 Invasion; intracellular multiplication observed for selected strains
Bladder
Urethra
1 Contamination of periurethral area with uropathogenic E. coli that has colonized the bowel
7 E. coli ascends to kidney
9 Cytokines induced
11 Sat vacuolates epithelial cell and damages glomeruli
5 Influx of PMNs
4 Apoptosis and exfoliation of bladder epithelial cells
2 Adherence to uroepithelial cells by type 1 and P fimbriae

Nature Reviews | Microbiology

Urinary Pathogens

Most UTIs are caused by facultative anaerobes usually originating from the bowel flora

- can get infections from flora of vagina or perineal skin } eg Staph epidermidis or Candida albicans

- **Most common cause by far is E coli**
    - community-acquired
        - E coli (85%), other G-ve } Proteus, Klebsiella,
        - G+ve } E. faecalis, S. saprophyticus (usually females)
- Nosocomial infections
    - E coli (50%)
    - Klebsiella, Enterobacter, citrobacter, serrratia, Pseudomonas, Providencia, E faecalis, S epidermidis (females)
- **Fastidious Organisms**
    - **Anaerobes in the Urinary Tract**
        - Uncommon. However, the distal urethra, perineum, and vagina are normally colonized by anaerobes.
        - often found in suppurative infections such as scrotal abscess, prostatic abscess, perinephric abscess
    - ***Mycobacterium tuberculosis* and Other Nontuberculous Mycobacteria**:
        - *Mycobacterium tuberculosis* and other nontuberculous mycobacteria, if cultures for acid-fast bacteria requested
    - **Chlamydia** less common
- Others: Gardnerella vaginalis, Mycoplasma species, Ureaplasma urealyticum, Bacteroides, Clostridium perfringens

Factors associated with successful infection of GU tract:

- ♥ Virulence factors
- ♥ Inadequate host defense mechanism.
- ♥ Inoculum size

Bacterial virulence

- Virulence characteristics determines
  - If an organism will invade the urinary tract and
  - The subsequent level of infection within the urinary tract.

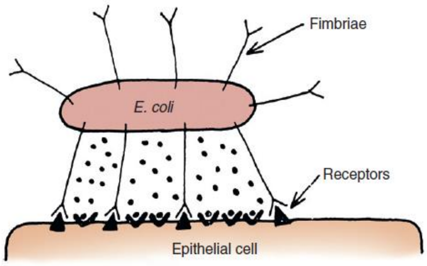


Figure 10–5. Bacterial adherence. Adhesins on pili (fimbriae) mediate attachment to specific epithelial cell receptors.

- Uropathogenic strains resident in the bowel flora, such as uropathogenic *E. coli* **(UPEC)**, → expression of virulence factors → adhere to and colonize the perineum and urethra → migrate to the urinary tract → UTI.

Bacterial virulence factors:

- **H**emolysin & mannose-resistant **H**emagglutination (**MRHA**)

- **P**ili or fimbriae (type 1 pili, P pili, S Pili)

- **O** antigen (cell wall)

- **K** antigen

- **E**xotoxin, **U**rease **or S**iderophore production

Bacterial Adhesin:

- ➢ **UPEC expresses a number of adhesins that allow it to attach to urinary tract tissues**

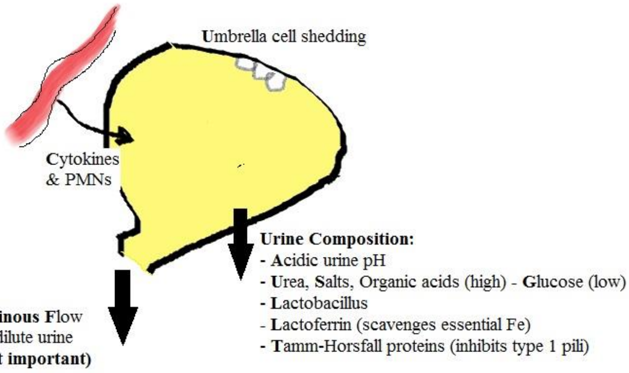
- Adhesins are classified as either fimbrial or afimbrial, depending on whether the adhesin is displayed as part of a rigid fimbria or pilus. Pili formed of subunits known as pilin.
- Pili are defined functionally by their ability to mediate hemagglutination of specific types of erythrocytes.
- The most well-described pili are types 1, P, and S.
    - type 1 pili
        - facilitates bacterial colonization of vaginal mucosa **&** **bladder**
        - helical rod composed of repeating FimA and FimH subunits
        - **FimH interact with receptors on bladder epithelium (uroplakins) → bacterial colonization & infection**
    - P pili
        - facilitates bacterial adherence to **kidney**
        - not associated with renal scarring or reflux
    - S pili
        - bind to bladder and kidney epithelial cells

Afimbrial adhesins (AFA)

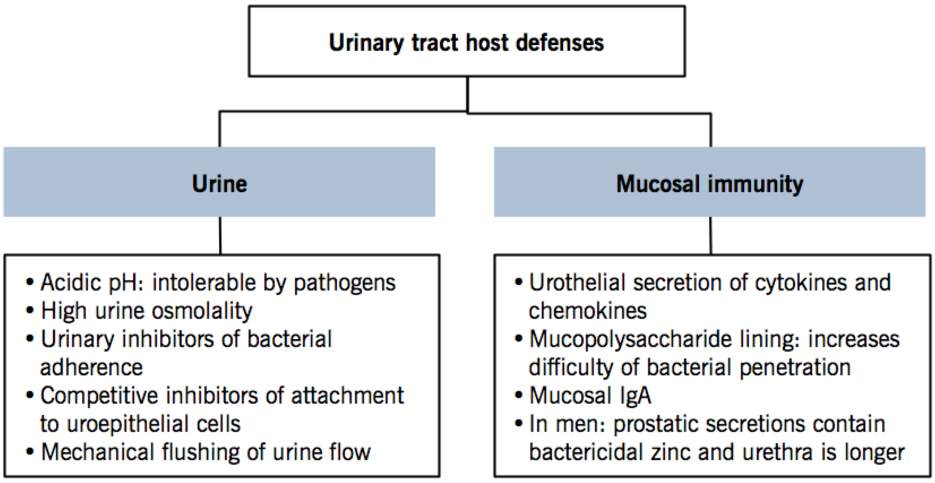
- expressed by UPEC

Inadequate host defense mechanism:

Host/urinary defence factors (inhibit bacterial growth):


Umbrella cell shedding
Cytokines & PMNs
Urine Composition:
- Acidic urine pH
- Urea, Salts, Organic acids (high) - Glucose (low)
- Lactobacillus
- Lactoferrin (scavenges essential Fe)
- Tamm-Horsfall proteins (inhibits type 1 pili)
Continous Flow of dilute urine (most important)

Urinary tract host defense mechanisms



- Acidic pH: intolerable by pathogens
- High urine osmolality
- Urinary inhibitors of bacterial adherence
- Competitive inhibitors of attachment to uroepithelial cells
- Mechanical flushing of urine flow

- Urothelial secretion of cytokines and chemokines
- Mucopolysaccharide lining: increases difficulty of bacterial penetration
- Mucosal IgA
- In men: prostatic secretions contain bactericidal zinc and urethra is longer

Risk Factors alter host defense mechanisms (increase UTI Risk):

- Local Causes:
  - ✓ Obstruction
    - ▪ urine stasis increases bacterial growth and adherence
    - ▪ stasis is not predisposing factor } **needs inoculum of bacteria**
  - ✓ VUR → unclear (but increase risk of pyelonephritis)
  - ✓ Pregnancy→ ~5% bacteriuria→no ttt→~30% acute pyelonephritis.
  - ✓ SCI
    - ▪ highest severity and morbidity of UTIs
    - ▪ Bladder overactivity or flaccidity complicates UTIs
- Systemic diseases:
  - Result in papillary damage:
    - ○ DM, sickle cell, adult nephrocalcinosis, hyperPO4, hypoK, analgesic abuse, gout, sulfonamide nephropathy, heavy-metal poisoning, aging.
  - Others: HTN, vascular obstruction, HIV….

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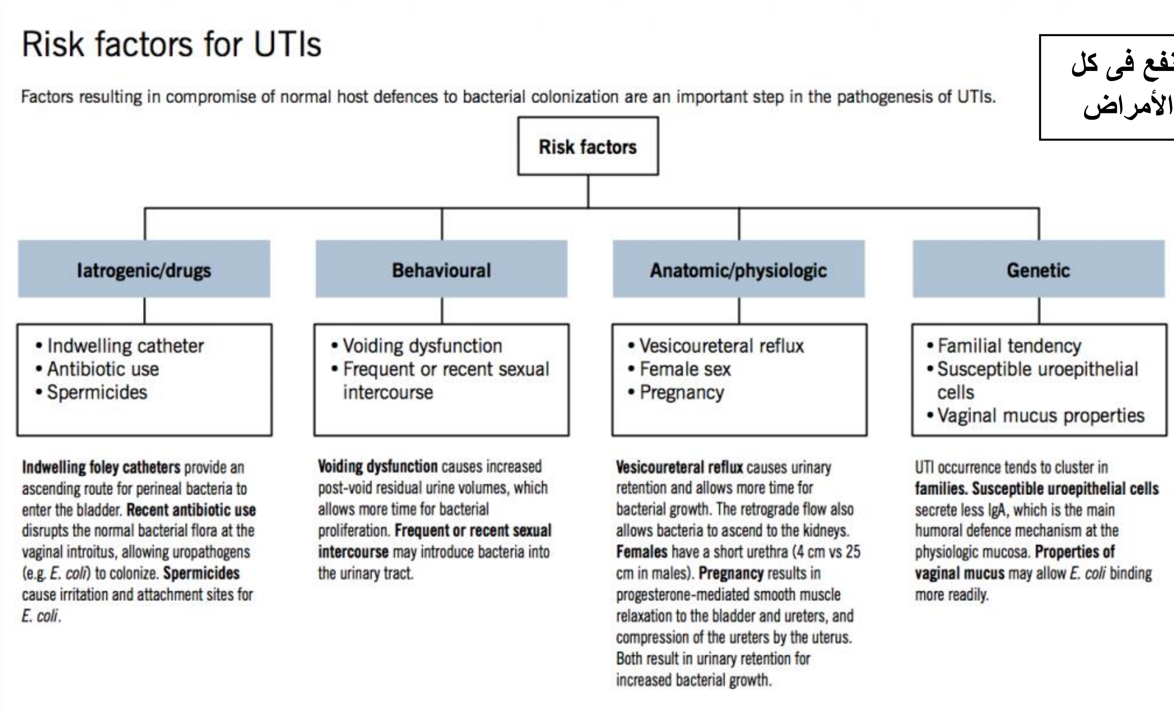


Risk factors for UTIs

Factors resulting in compromise of normal host defences to bacterial colonization are an important step in the pathogenesis of UTIs.

Risk factors

Iatrogenic/drugs

- Indwelling catheter
- Antibiotic use
- Spermicides

Indwelling foley catheters provide an ascending route for perineal bacteria to enter the bladder. **Recent antibiotic use** disrupts the normal bacterial flora at the vaginal introitus, allowing uropathogens (e.g. *E. coli*) to colonize. **Spermicides** cause irritation and attachment sites for *E. coli*.

Behavioural

- Voiding dysfunction
- Frequent or recent sexual intercourse

Voiding dysfunction causes increased post-void residual urine volumes, which allows more time for bacterial proliferation. **Frequent or recent sexual intercourse** may introduce bacteria into the urinary tract.

Anatomic/physiologic

- Vesicoureteral reflux
- Female sex
- Pregnancy

Vesicoureteral reflux causes urinary retention and allows more time for bacterial growth. The retrograde flow also allows bacteria to ascend to the kidneys. **Females** have a short urethra (4 cm vs 25 cm in males). **Pregnancy** results in progesterone-mediated smooth muscle relaxation to the bladder and ureters, and compression of the ureters by the uterus. Both result in urinary retention for increased bacterial growth.

Genetic

- Familial tendency
- Susceptible uroepithelial cells
- Vaginal mucus properties

UTI occurrence tends to cluster in **families. Susceptible uroepithelial cells** secrete less IgA, which is the main humoral defence mechanism at the physiologic mucosa. **Properties of vaginal mucus** may allow *E. coli* binding more readily.

- **Inoculum size**

Microbiological and other laboratory findings

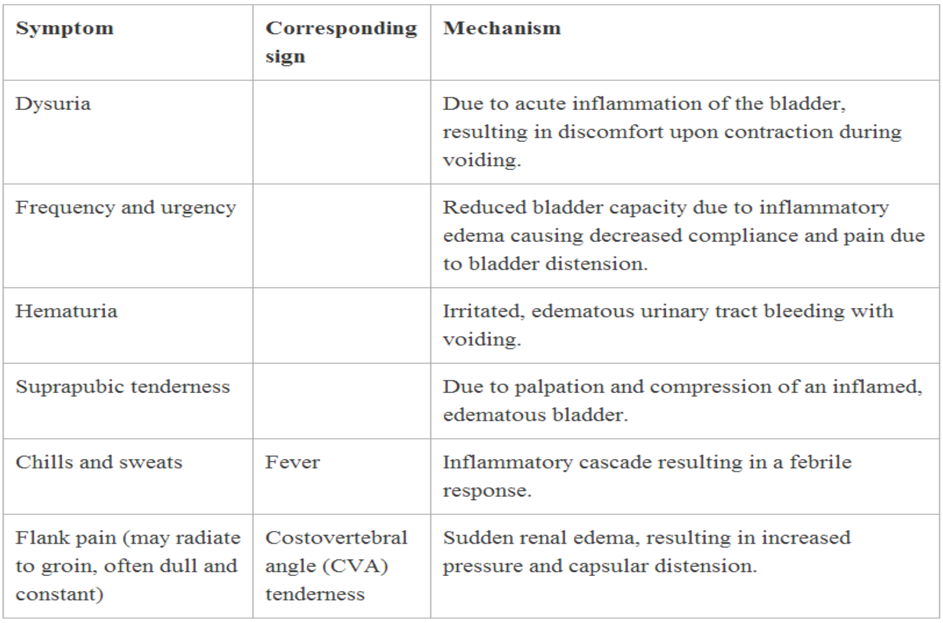
- the following bacterial counts are clinically relevant:
  - 10^3 cfu/mL in a mid-stream sample of urine (MSU) in acute uncomplicated cystitis or pyelonephritis (10^4) in women
  - 10^5 cfu/mL in an MSU in women, or $\geq 10^4$ cfu/mL uropathogens in an MSU in men, in a complicated UTI
  - In a suprapubic bladder puncture specimen, any count of bacteria is relevant.

Bacterial resistance development

- **Extended-spectrum β-lactamase (ESBL) producing bacteria** resistant for most antibiotics (except carbapenem).
- Some faecal bacteria produce **ESBL$_{\text{CARBA}}$ enzyme** (resist all).
- Resistance to Overuse of broad-spectrum antibiotics (as fluoroquinolones and cephalosporins) → resistance to them **and** parallel co-resistance to other antibiotics **(Collateral damage)**

Clinical presentation

- No clinically specific symptoms.
- Elderly women may present with only urinary incontinence.



Symptom	Corresponding sign	Mechanism
Dysuria		Due to acute inflammation of the bladder, resulting in discomfort upon contraction during voiding.
Frequency and urgency		Reduced bladder capacity due to inflammatory edema causing decreased compliance and pain due to bladder distension.
Hematuria		Irritated, edematous urinary tract bleeding with voiding.
Suprapubic tenderness		Due to palpation and compression of an inflamed, edematous bladder.
Chills and sweats	Fever	Inflammatory cascade resulting in a febrile response.
Flank pain (may radiate to groin, often dull and constant)	Costovertebral angle (CVA) tenderness	Sudden renal edema, resulting in increased pressure and capsular distension.

Investigations:

- Urine dipstick test showing **positive nitrites** or **leukocyte esterase** are suggestive of UTI, raising the pretest probability by 25%.
    - Nitrite:
        - positive due to bacterial reduction of endogenous nitrates to nitrites; classically positive in G-ve Enterobacteriaceae family.
    - Leukocyte esterase:
        - positive as neutrophil granules contain enzymes with esterase activity; presence of neutrophils in urine due to UTI.
- Only a **positive urine culture** is truly diagnostic of a UTI.

UTI

Bladder Infections:

- Uncomplicated cystitis
- Complicated Cystitis.
- Emphysematous cystitis.

Renal infections:

- Acute pyelonephritis.
    - Complicated
    - Uncomplicated
- Acute focal or multifocal Bact. Nephritis (Lobar nephronia).
- Chronic pyelonephritis.
- Xanthogranulomatous pyelonephritis.
- Emphysematous Pyelonephritis.
- Renal abscess.
- Perinephric abscess & Paranephric abscess
- Pyonephrosis.
- Malacoplakia.

Specific Infections

- Tuberculosis
- Parasitic infection
    - Schistosomiasis
    - Amebiasis
    - Renal Echinococcosis.
- Fungal infection
- Sexually transmitted diseases
    - Including HIV infection

Specific situations

- UTI in pregnancy
- UTI in elderly
- UTI in children
- UTI (catheter associated)

Other Infections:

- Fornier's gangrene
- Periurethral abscess

Inflammatory conditions of Male genitourinary tract:

- Prostatitis
- Orchitis
- Epididymitis

Sepsis conditions:

- Bacteremia
- Sepsis
- Septic shock

BLADDER INFECTIONS

Uncomplicated cystitis

Incidence:

- 10% of women per annum and 50% of women during their lifetime
- rare in young men, without structural or fxn’al abnormalities (cystitis considered COMPLICATED in men until proven otherwise)

Pathogenesis:

العامة وشوية
حاجات مميزه

- **Risk Factors:**
  - reduced urine flow
    - **BOO** (BPH, PCa, urethral stricture, stone)
    - **Neurogenic bladder**
    - dehydration
    - urethral diverticulum
  - colonization risk
    - **sexual activity**
    - **spermicide use** (increased bacterial binding)
    - **estrogen-depletion** eg menopause (increased bacterial binding)
    - Abx use (decreased natural flora)
  - facilitation of ascent
    - catheterization
    - incontinence (urine or fecal)
    - **residual urine with bladder wall ischemia**
- Causative organisms:
  - Female: **E. coli** ~90% in young women,
    S. saprophyticus ~10-20%
  - Male: E. coli and other enterobacteriaceae most common

C/P:

- dysuria, frequency, urgency
- S/P pain
- hematuria
- foul-smelling urine
  - ➔ **NO fever, chills**

Investigations:

- Lab:
  - U/A: pyuria, bacteriuria, hematuria
  - urine C&S: >10^2 cfu/mL in symptomatic pts (NOT RECOMMENDED IN ALL PTS)

DD (of dysuria):

- vaginitis
- urethral infections (gonorrhea, Chlamydia, herpes, trichomoniasis)
- noninflammatory urethritis
- CIS of bladder

Treatment:

- Abx:
  - women
    - 3days of cipro, levo, Septra DS, Trimethoprim, Macroid, norflox
    - 7days of Septra DS or cipro **if**
      DM, >65yrs, >1wk of symptoms, recent UTI, or use of diaphragm
  - pregnancy
    - 7 days of amoxicillin, Keflex, nitrofurantoin, Septra (only in 2nd trimester)
  - men
    - 7days of Septra DS or cipro

Complicated cystitis

Treatment:

- correct any underlying GU tract abnormalities
    - if mild to moderate
        - 10-14days of cipro or Septra DS
        - commonly E. coli, Proteus, Klebsiella, or Pseudomonas
    - if severe
        - iv amp + gent, cipro, ceftriaxone until afebrile
        - step-down to 14-21days of po cipro, Septra DS, levo (or culture-guided Rx)
        - post-Abx urine C&S

Emphysamatous Cystitis

Risk factors:

- DM
- Elderly, Female
- immunocompromised
- recurrent UTIs
- retention/neurogenic bladder

DD (of air in the bladder):

- instrumentation
- fistula } malignancy, colitis, iatrogenic, etc
- gas forming UTI } E. coli, Clostridium, enterobacter, Proteus, etc

Treatment:

☑ **foley drainage**
☑ **broad spectrum Abx**
☑ **control of DM (glucosuria)**
☑ **+/- anti-fungals if yeast cultured**

KIDNEY INFECTIONS

Common C/P:

extremely variable (from cystitis, mild flank pain to gram-negative sepsis)

- ➢ fever, chills, flank pain + irritative symptoms } may not be present, esp in DM, elderly, SCI
- ➢ GI symptoms of N/V, abdo pain, diarrhea } may be asymptomatic

Investigations

- ▪ urine analysis and culture
    - o bacteriuria and pyuria with large amounts of WBC casts
    - o may be negative if ureter is obstructed or if infection is not in collecting system → ~20% can have negative urine C&S
- ▪ +ve blood culture in ~25% and usually same urine C&S results
- ▪ may not have renal impairment (variable)

Acute pyelonephritis

Pathogenesis:

- Route of infection and ass. pathology:
    - hematologic dissemination
        - multiple focal areas of suppuration on surface of kidney
        - focal destruction of glomeruli and tubules
        - rest of cortex and medulla are NOT involved
    - ascending infection
        - linear bands of inflammation from medulla to renal capsule
        - focal wedge-shaped area of acute interstitial inflammation
        - PMN leukocytes or plasma cells +/- bacteria
    - chronic pyelo
        - cortical scar associated with retraction of corresponding renal papilla
        - patchy involvement with numerous chronic inflammatory foci
        - normal glomeruli outside scarred areas
        - papillary deformity, sclerosis and sometimes necrosis

Causative organisms:

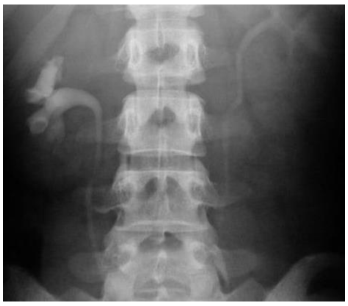
- E coli represents ~80%
- Proteus, Klebsiella, Pseudomonas
- Enterobacter
- S.epidermidis/S.aureus
- E. faecalis

Inv.

- ➢ Rad.:

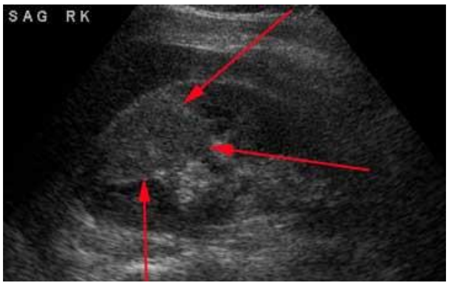
  ➔ most cases have N imaging

1) IVP (75% N)



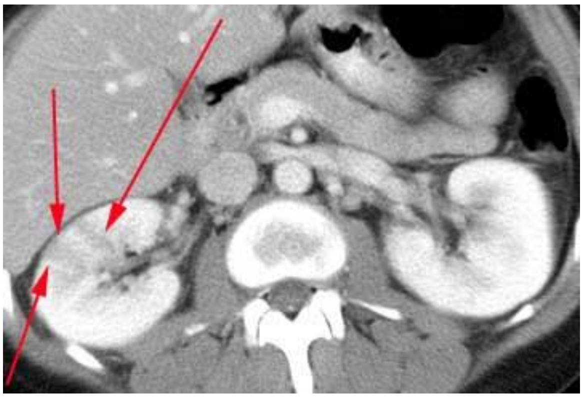
- renal enlargement (>15cm or >1.5cm compared to other side) **most common abN**
- delayed excretion
- compressed collecting system (eg spidery calyces)
- ureteral dilatation (endotoxin-mediated impairment of peristalsis)

2) ultrasound (usually N)



- renal enlargement } most common abN
- hypoechoic parenchyma
- compressed collecting system
- may see abscess

3) CT



- renal enlargement
- streaky hypoattenuation of renal parenchyma } most common
- perinephric stranding (or even perinephric abscess)
- cortical striations
- Compressed or dilated collecting system (hydronephrosis)
- urothelial thickening
- paraureteral or parapelvic lucency

TTT:

Acute pyelonephritis does not cause scarring in normal GU tract

1) uncomplicated (no sepsis, no N/V)

- urine culture
- +/- imaging (U/S or CT to r/o stones or obstruction)
- outpt Abx for 10days (cipro / Septra DS)
    - if NO improvement, admit, review cultures, start iv Abx, r/o obstruction or abscess
    - if improvement, culture after ABx’s + urologic evaluation

2) complicated or sepsis □ blood & urine cultures

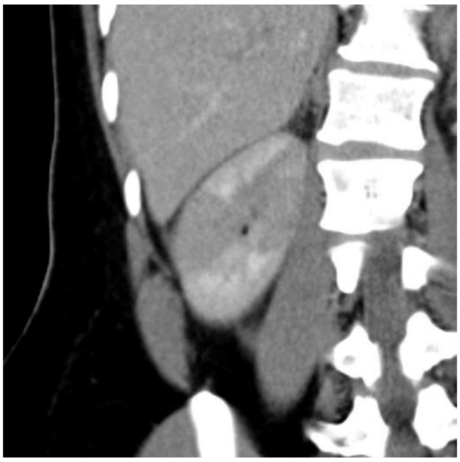
- ✓ imaging
- ✓ iv Abx (cipro / amp + gent / ceftriaxone) x 3days } 7 days if +ve blood C&S
    - ➔ if NO improvement, r/o abscess or persistent obstruction, re-culture
    - ➔ once afebrile, po Abx for 10-14 days (cipro / Septra DS / Keflex)
- ✓ culture after Abx therapy (at 2weeks then again at 4-6 weeks)

Acute Focal or Multifocal Bacterial Nephritis (Lobar nephronia)

➔ uncommon, severe form of acute renal infection

Differ from acute pyelonephritis in:

- infection confined to single renal lobe or multiple lobes
- more severe than acute pyelo → 50% are DM, 50% are bacteremic, sepsis common
- likely an early phase of frank renal abscess



INV.

- CT:
  - non-enhancing area
  - wedge-shaped lesion in kidney
  - poorly marginated
  - mass effect within kidney (can resemble tumour)

ttt:

- hydration
- iv Abx for x ≥ 7days, then po Abx for 7days
- if no improvement, need to r/o obstruction, abscess, RCC

➔ usually responds to medical therapy

Chronic Pyelonephritis

Incidence:

- rare in patients without underlying renal or GU tract disease

C/P:

- **Intermittent symptoms** of fever, flank pain, dysuria (if due to recurrent episodes of acute pyelo).
- usually **asymptomatic** until in renal failure
- usually ass. with rec. UTIs, VUR, analgesic abuse, stones, or obst.
- causes **ESRD** in patients with underlying renal or GU tract disease
- **NOT associated with HTN**

Inv.:

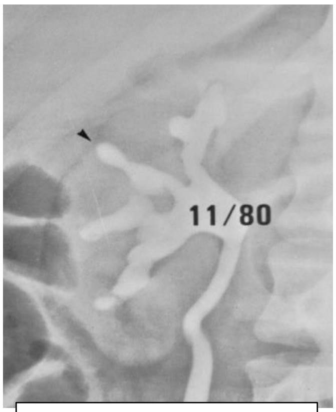
➢ Lab.
  - bacteriuria and pyuria are not predictive of renal infection

  ➔ Sterile urine if obst. Ureter or inf. outside the collecting system

➢ Rad.

IVP:

  - Small, irregular & atrophic kidneys.
  - blunting & dilation of ≥1 calyces with cortical scars overlying it.
  - compensatory hypertrophy contralat. kidney



irregular renal outline with scarred parenchymal overlying dilated calyx

DDx (dilated calyx with scarring of overlying cortex):

- chronic pyelo
- analgesic nephritis with papillary necrosis
- stones/obstruction of calyx
- renal infarction
- TB

ttt:

- ○ Abx (C&S), prolonged, and not nephrotoxic
- ○ in N urinary tracts, recurrent UTIs are NOT caused by relapse from bacterial persistence in renal parenchyma

Xanthogranulomatous Pyelonephritis (XGP)

Def.:

- a rare, severe, chronic renal infection typically resulting in diffuse renal destruction

Incidence:

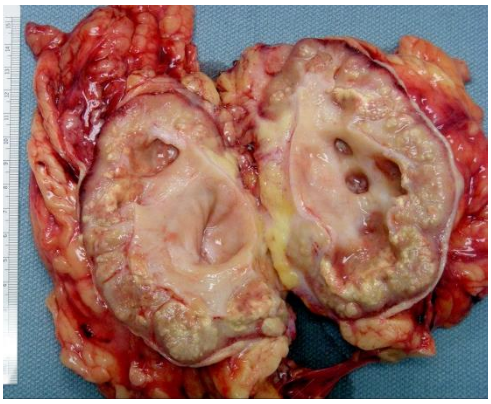
- more common in women and DM
- usually unilateral } so renal failure uncommon
- usually presents in 40’s to 60s

Pathogenesis:

- ➢ Causes
  - Primarily involves **stones + obstruction + infection**
  - may also involve:
    - venous occlusion and hemorrhage
    - lymphatic blockage
    - altered immunologic competence
    - abnormal lipid metabolism
    - failure of Abx therapy for UTI
    - renal ischemia

- ➢ Causative organism:
  - bacteria are usually of low virulence } bacteremia rare
  - **Proteus** is most common organism (E coli also very common)

- Pathology:
  - usually unilateral → non-functioning, enlarged kidney associated with obstructive uropathy secondary to stones
  - characterized by accumulation of **lipid-laden foamy macrophages (xanthoma cells)**
  - can resemble RCC
  - XGP kidey:
    - massively enlarged with normal contour} diffuse (~80%)
    - has stones and peripelvic fibrosis (fibrosis prevents pelviectasis).
    - starts within pelvis and calyces → destroys parenchyma and near tissues → dilated calyces filled with purulent material
    - papillary necrosis
    - in advanced disease, multiple abscesses, thinned parenchyma

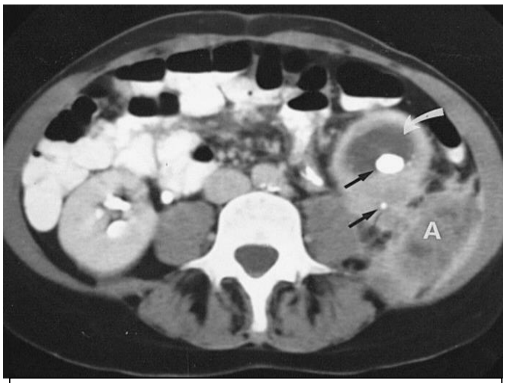


C/P:

- classic triad
  - **unilateral enlargement**
  - **non-functioning or poorly functioning kidney**
  - **large stone in renal pelvis**
- Renal mass: indistinguishable from malignant tumour
- Others
  - flank pain, fever, and chills 70%
  - persistent bacteriuria 50%
  - flank mass 60%
  - hx of stones 35%
  - malaise, anorexia, wt loss, Hx of UTIs
- HTN, hematuria, and hepatomegaly (rarely)

Inv.:

- Lab.:
  - U/A: pyuria and proteinuria
  - anemic, hepatic dysfunction
- Rad.:
  - Radiological Chch.
    - unilateral enlargement
    - renal pelvic stone
    - poorly functioning or nonfunctioning kidney
    - may resemble mass
  - **CT scan:**
    - ideal imaging modality
    - contrast CT may show ulcerated pyelocalyceal system with multiple irregular fillind defects
    - large reniform mass w/ renal pelvis tightly surrounding a central calcification but without pelvic dilatation
    - **renal parenchyma is replaced by multiple water-density masses (dilated calyces & abscesses) filled with debris and pus**
    - enhancement of wall of abscess cavities but cavity itself doesn't enhance



stones (black arrows) with LP pyonephrosis (curved arrow) + perinephric abscess (A)

- U/S
  - global enlargement of kidney
  - normal renal tissue replaced by multiple hypoechoic fluid-filled masses
  - stone in collecting system
- renal scan
  - DMSA used to quantify differential lack of function

DDx

- pyonephrosis } usually doesn’t have stones
- renal malacoplakia } usually don’t have stones
- renal lymphoma } usually bilateral and not associated with stones
- RCC } can resemble clear cell RCC on frozen section

ttt:

→ often wrongly diagnosed

- **Abx** } usually peri-op … but occasionally, long-term ABx may eradicate infection & restore renal fxn
- **Partial Nx** for localized XGP
- **Nx for diffuse XGP** } open approach recommended
- **Radical Nx**
  - if RCC suspected } has been associated with RCC, papillary TCC of the renal pelvis or bladder infiltrating SCC of pelvis.

Emphysematous pyelonephritis

Def.

- acute necrotizing parenchymal & perirenal infection caused by gas-forming organisms

Incidence

- all in adults, women more commonly (6x)
- complication of severe pyelonephritis } overall mortality ~20-40%

Pathogenesis:

- usually occurs in DM
- obstruction with stones or papillary necrosis common only in NON-DM's

- Causative organism:
  - E. coli (Klebsiella also).

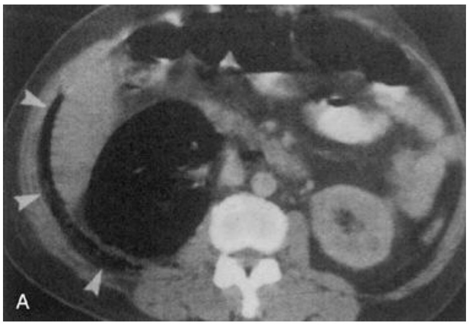
C/P:

- most have triad of fever, N/V, and flank pain

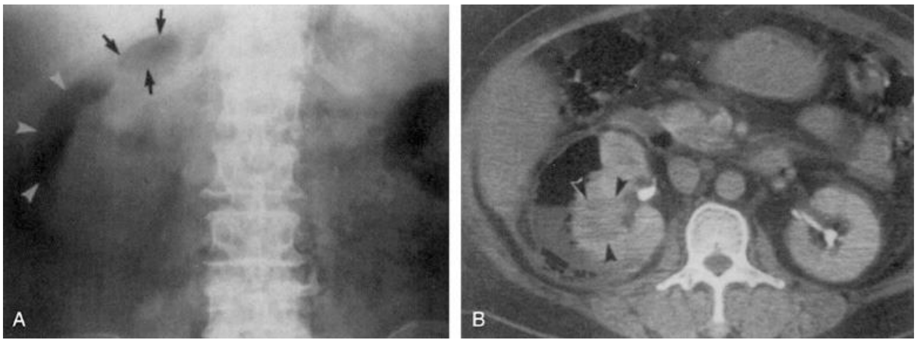
INV.:

- Rad.:
  - obstruction seen in ~25%
  - U/S shows strong focal echoes suggesting intraparenchymal gas
  - **CT is imaging modality of choice**

☑ Radiological classification



- Type I } 50% mortality rate
    - **no fluid** in renal or perinrenal tissue
    - streaky or mottled **gas in** or around kidney +/- gas in collecting system
    - +/- bubbly or loculated gas in collecting system
    - **complete destruction of kidney**
- Type II } 20% mortality rate
    - + ve renal or perirenal fluid
    - no streaky or mottled gas in kidney
    - + bubbly or loculated gas in collecting system



ttt:

Can be a surgical emergency } most pts are septic

- hydration
- broad-spectrum iv Abx
- relief of obstruction if present } drainage
- Nx if type I or no signs of improvement after a few days of therapy
    - indications for immediate Nx:
        1) type 1
        2) no improvement with conservative therapy
        3) critically ill + ARF/shock/thrombocytopenia/mental status changes

☐ unless bilateral } trial of drainage + iv Abx

Renal Abscesses

Def.:

- collection of purulent material confined to renal parenchyma

Pathogenesis:

- Predisposing factors:
  - iv drug use
  - skin carbuncles
  - recurrent lung infections
  - complicated UTIs associated with:
    - stasis
    - stones
    - DM
    - pregnancy
    - neurogenic bladder
- Causative organism:

- usually due to G –ve bacteria (used to be gram +ve before Abx)
  - usually from ascending infection associated with tubular obstruction from prior infections or stones
  - 2/3 of gram –ve abscesses are associated with stones or damaged kidneys
- gram +ve abscesses (usually from bloodborne sources)

C/P:

- may have a hx of a recent gram +ve infection (1-8weeks) before GU tract symptoms
- may present with fever, chills, abdo pain or flank pain (may have wt loss and malaise)

Inv.:

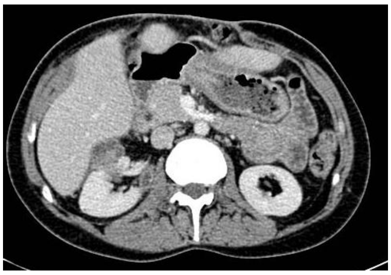
- Lab.:
  - marked elevation in WBC
  - pyuria and bacteriuria usually absent if gram +ve (bloodborne) abscess
  - +ve blood cultures

- Rad.:

hard to differentiate early renal abscess from acute pyelonephritis

1. IVP:
   - IVP finding of **acute** renal abscess:
     - generalized renal enlargement
     - distortion of renal contour
     - renal fixation with respiration
     - obliteration of corresponding psoas shadow
     - delayed or absent nephrogram if diffuse renal involvement
   - IVP findings of a chronic renal abscess:
     - renal mass lesion
     - poorly defined or distorted calyceal system
     - radiolucency in affected area on nephrotomogram
2. PAU/S
   - U/S findings suggestive of a renal abscess:
     - hypoechoic or echo-free space-occupying lesion with increased transmission
     - poorly marginated
     - strong internal echo with shadow if air

3. CT (of choice):
   - CT findings suggestive of a renal abscess:
     - well defined pre and post-contrast
     - early } renal enlargement with focal, rounded areas of hypoattenuation
     - later
       - ring-enhancing thickened-wall with hypoattenuating parenchymal mass
       - obliteration of adjacent tissue planes and thickening of Gerota's fascia



ttt:

☑ **FNA if suspicious of a hypervascular tumour**

☑ General therapies:

- iv Abx
- hydration
- serial reimaging

☑ **perc drainage if:**

<3cm in immunocompromised pt

>3cm (consider open drainage if >5cm)

no response to Abx

☑ Antibiotic regimen:

- Hematogenous origin → cephalosporin or vancomycin
- G –ve suspect → 3rdG cephalosporin, ampicillin, gentamicin

Pyonephrosis

Def.:

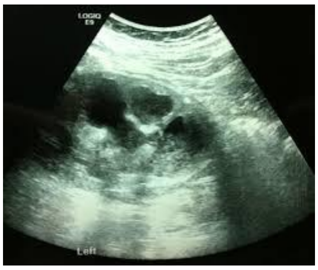
- ♥ **infected hydonephrosis** associated with **suppurative destruction of renal parenchyma** with total or nearly total loss of renal f.
- ♥ Early Dx and treatment to avoid sepsis and permanent renal f loss.

C/P:

- very ill patient with high fever, chills, flank pain and tenderness
- may occasionally present with fever and vague GI symptoms
- common to have hx of stone, UTI, or GU tract surgery

Inv.:

- ➢ Lab: No bacteriuria if ureter is completely obstructed
- ➢ Rad.:
  1) U/S
     - internal echoes within dependent portion of dilated pyelocalyceal system
     - focal areas of decreased echogenicity within hydronephrotic parenchyma



  2) CT } nonspecific
     - poorly functioning kidney with thinned parenchyma.
     - Pelvicaliectasis.
     - may show thickening of renal pelvis, perinephric stranding, and striated nephrogram.

ttt:

- iv Abx
- drainage of infected renal pelvis
- once stable, find source of obstruction

Perinephric abscesses

Pathogenesis:

- Risk factors:
  - DM present in ~1/3 of cases
  - pyonephrosis or perinephric hematoma
  - PCKD on HD
- Causes of perinephric abscesses:
  - bowel perforation
  - Crohn’s disease
  - spread of osteomyelitis from thoracolumbar spine
- Route of infection: either
  - rupture of acute renal abscess **or** hematogenous seedin
- Causative organism:
  - usually E coli, Proteus, and S aureus

C/P:

- often insidious onset

- similar presentation to pyelonephritis but often afebrile (30%).

- abd. or flank mass palpable (~50%).

- Psoas abscess may present with **a limp and flexion and external rotation of ipsilateral hip**

Inv.:

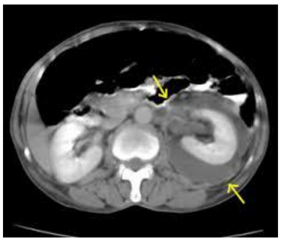
- Lab.: elevated WBC, elevated creatinine, pyuria found in 75%
- Rad.:

  1) IVP
     - abnormal in 80% of cases, but nonspecific abnormalities
     - absence of psoas shadow, mass in perirenal area, blurred renal outline, and elevated or immobile diaphragm
     - Extraluminal gas around kidney if gas-forming organism

2) ultrasound
   - variable
   - ranges from anechoic mass displacing kidney to echogenic collection that blends with normally echogenic fat within Gerota's fascia
3) CT
   - **primary modality of choice**
   - shows primary abscess and route of spread of infection

ttt:

➔ if symptomatic for >5days or febrile despite Abx for >4days, think abscess



- **Abx** based on urine & blood cultures may often be **inadequate**
  - predicts abscess organism only ~50% of the time
  - usually doesn't respond to Abx alone
- **perc drainage** of small collections.
- **open surgical drainage** (or Nx if nonfunctioning or severely infected) for larger collections
- **treatment of underlying problem**

➔ delay in Dx is often the main reason for high morbidity associated w/ perinephric abscesses

PARA-nephric abscess:

- perinephric infection that has ruptured through Gerota's fascia or from other local sources
- Or from infectious disorders of the bowel, pancreas, or pleural cavity

Malacoplakia

Def.:

- inflammatory disease that can affect entire GU tract, GI tract, skin, lungs, bones, & mesenteric LNs

Incidence:

- >50yrs old, F:M 4:1 (only seen in GU tract malacoplakia).
- mortality can be >50%

Pathogenesis:

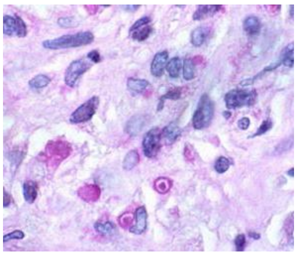
- can occur in almost **any organ** BUT **75% are GU** (bladder most common, then kidney)
- D.t from abn macrophage function in response to bacteria } usually **E.coli** (imbalance cGMP/cAMP→v.low cGMP & v.high cAMP).

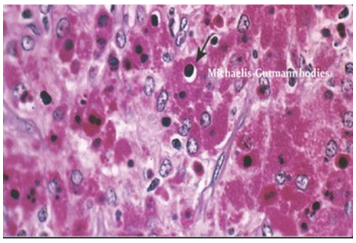
➢ Causative organism:

- Usually E-coli
- unknown } ?coliform bacteria in immunocompromised pts (AIDS, autoimmune disease, Ca, etc) → likely involves defect in bacterial digestion with unusual immunologic response.

➢ Pathology:

- Gross:
    - soft, yellow-brown plaques with granulomatous lesions with Michaelis-Gutmann bodies
- Microscopic:
    1. large histiocytes (von Hanselmann cells)
    2. small basophilic granules **(Michaelis-Gutmann bodies)**





- pathognomonic but NOT essential
- contain large amounts of immunoreactive α1-antitrypsin
- incompletely destroyed bacteria surrounded by lipoprotein membrane.
- laminated lysosomal inclusion bodies (laminated in Ca PO4 crystals)

C/P:

➔ usually immunosuppressed or debilitated } persistent coliform UTIs in ~90% (E. coli)

Ca deposition within MQ

☑ bladder

- irritative symptoms with hematuria & smooth filling defects in bladder

☑ renal malacoplakia

- associated with renal vein thrombosis & IVC thrombosis

☑ testicular malacoplakia

- associated with epididymo-orchitis

Inv.:

- **Diagnosis made on biopsy**
- Lab. Urine analysis and culture
- Rad.
  - renal malacoplakia?
    - multifocal malacoplakia
      - usually presents as enlarged kidneys with multiple filling defects
      - NO renal calcifications, stones, or hydro
      - **on CT**, malacoplakia lesions are less dense than surrounding renal parenchyma

- unifocal malacoplakia
  - a noncalcified mass that is indistinguishable from other inflammatory or neoplastic lesions
  - **on CT**, may see solid or cystic structure, depending on degree of internal necrosis.

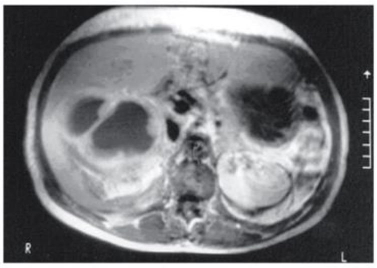


Figure 1 - Magnetic Resonance Imaging revealing a soft tissue mass in the right kidney

DDx:

- renal cystic disease (can tell with good CT)
- renal inflammatory disease
- RCC (not usually multifocal)
- XGP (usually have stones and UTI symptoms)

ttt: (Goal: control the UTIs → stabilize the disease process)

- **Renal malacoplakia**
  - **Antibiotics**
    - Septra DS, rifampin, doxycycline, and cipro recommended because of intracellular bactericidal activity
    - **cipro** good because taken up by macrophages
  - add **ascorbic acid & bethanechol**
    - to ↑ normal macrophage function (especially if NO UTIs)
  - Usually needs surgical ttt.
    - **Nx** recommended if in Tx kidney, multi-focal distribution or refractory to ABx
      (death w/in 6mos **if** B/L renal malacoplakia **or** in Tx Kid)
      (survival after nephrectomy good for unilateral renal dis.)
- **Bladder malacoplakia**
  - initially by **TUR + ABx**

Specific infections

TB, Parasitic, and Fungal Infections of the GU System

GU TUBERCULOSIS

Incidence:

- WHO (1/3 of world infected) but declining rates since early 90's.
- ~1% → GU tract is the primary site.
- ~20% only extrapulmonary disease (**5% of those have GU T.B)**
- Mostly 20-40y (uncommon in kids (**epididymis most common**)
- M:F 2:1

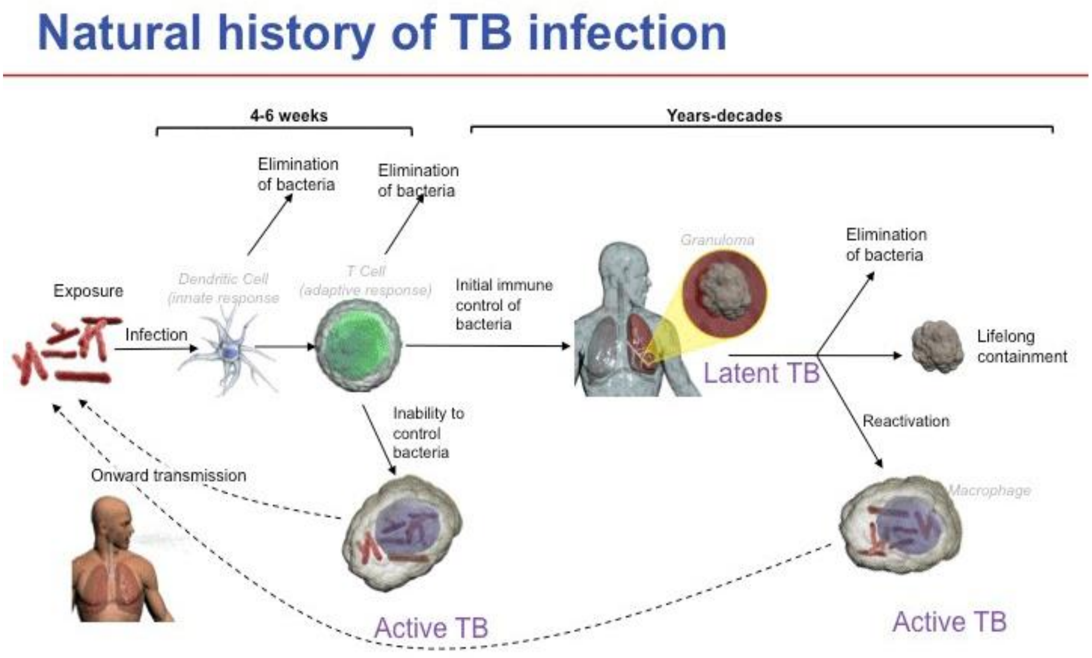
Pathogennesis:

- Causative organism: **Mycobacterium Tuberculosis**
  - Ultrastructure:
    - **small bacilli with thick wall**
    - non-motile (no true capsule or flagellum)
    - cell wall is complex structure made of 4 layers
      - peptidoglycan + 3 layers of peptides, polysaccharides, and lipids
  - organisms of the *M. tuberculosis* complex:
    - ***M. tuberculosis, bovis, microti and africanum***
    - *the non-tuberculous mycobacteria rarely cause disease in GU tract and often resistant to one or more of the 1st line drugs*
  - association of TB and HIV:
    - **TB (Most common opportunistic infection in AIDS Pts**)
    - almost all TB + HIV pts will develop active disease unless anti-TB prophylaxis taken

- Route of transmission:
  - **Inhalation:**
    - **almost all M. *tuberculosis* infections are acq'd by inhalation of aerosolized droplet nuclei**
    - **50% of the active disease occurs within 2yrs of infection**
    - Anti-TB prophylactic meds recommended if evidence of a new infection (conversion to +ve PPD) or heavy exposure**.**
  - **Bloodborne**:
    - metastatic spread of M. *tuberculosis* through blood during initial infection**.**
      - **kidney is the first GU organ involved** } can lie dormant in granulomas for yrs
      - other parts of GU involved by direct extension
      - **epididymis is the most common site in genital tract (fallopian tubes in women)**

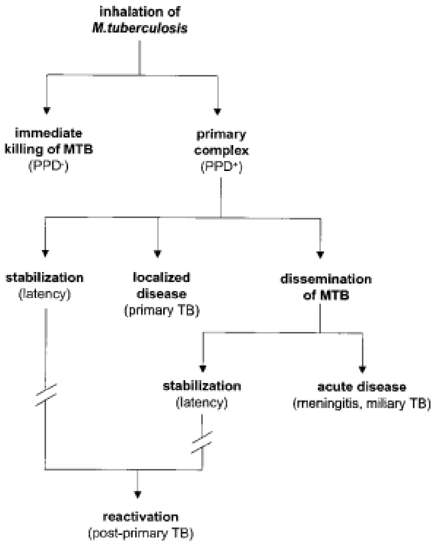
So renal TB can develop By:

- **activation of a prior bloodborne renal infection**
- organism settles in blood vessels close to glomeruli
- **caseating granulomas** develop & consist of **Langhans giant cells** surrounded by **lymphocytes & fibroblasts**


Natural history of TB infection

- Development of active TB:
  - depends on interaction between pathogen & host immune response
  - M. *tuberculosis* evokes both cellular & humoral immune response
  - T lymphocytes → cytokines → activate macrophages more mycobactericidal
  - **once macrophages are activated, initial infection is controlled & bacilli become dormant**

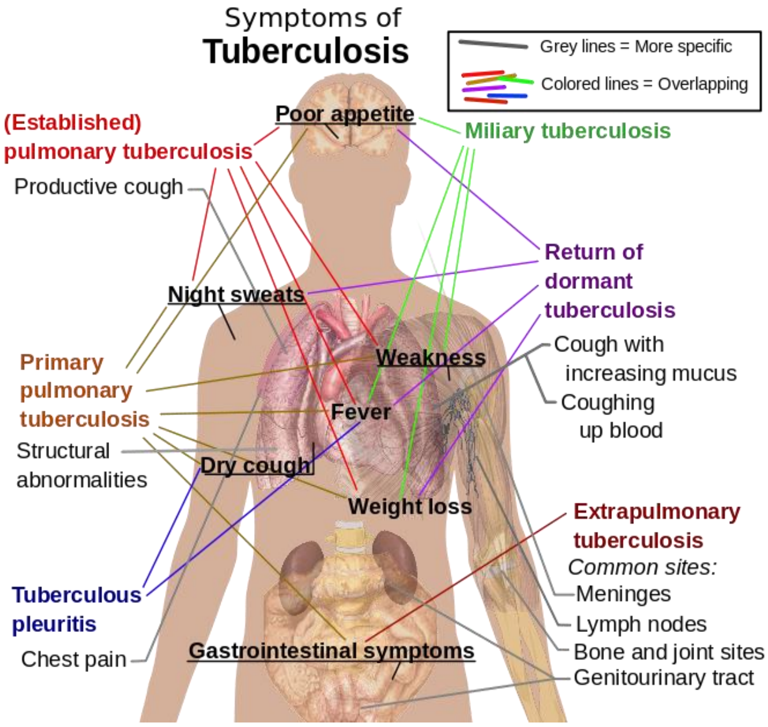
- **RFs for developing active TB after initial infection (reactivation of dormant TB:**
  - **D**M, **S**teroids, **I**mmunosuppressive therapy, **AIDS**
  - **D**ebilitating disease
  - **T**rauma


inhalation of M.tuberculosis
immediate killing of MTB (PPD-)
primary complex (PPD+)
stabilization (latency)
localized disease (primary TB)
dissemination of MTB
stabilization (latency)
acute disease (meningitis, miliary TB)
reactivation (post-primary TB)

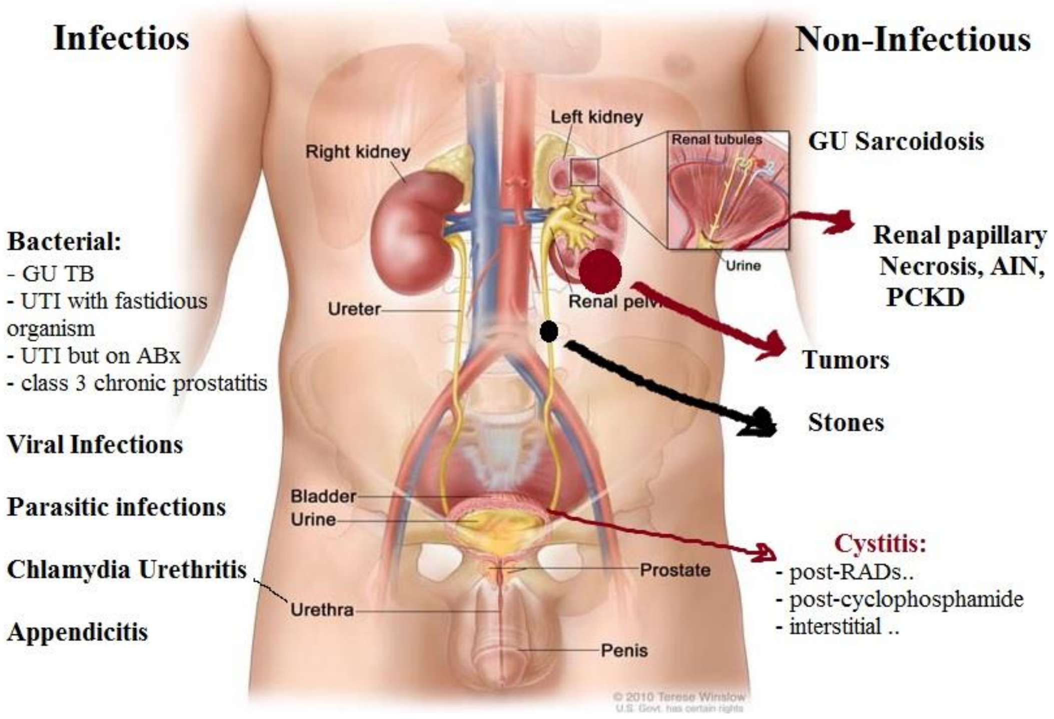
C/P:

- consider Dx when pt presents w/ vague, long-standing urinary symptoms w/ no obvious cause

- **LUTS (no dysuria), hematospermia, painful testicular swelling, S/P pain**
- **sterile pyuria**



DDx: causes of sterile pyuria



==

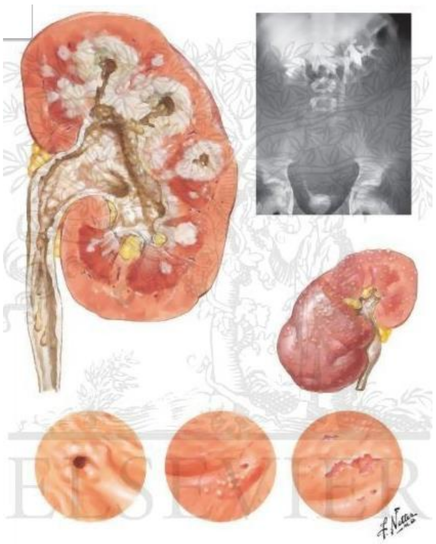
TB of the Kidney, Ureter, and Bladder

C/P: (Intermittent symptoms)

- **frequency** (painless),
- **cystitis** (recurrent)
- **renal or S/P pain** (rare and usually means extensive involvement of kidney and bladder)
- **sterile pyuria } classic finding, although 20% don't have leukocytes in urine**
- gross hematuria in only 10%, microscopic hematuria in 50%

Renal TB

complications of renal TB:



- Parenchyma:
  - caseating ***granulomas***, medullary ***nephrocalcinosis*** can lead to autonephrectomy and ***papillary necrosis*** (**earliest sign is calyceal contour abN'ities** due to papillary necrosis)
  - HTN
- PC system:
  - calyceal strictures (moth-eaten calyces), infundibular stenosis, hike up renal pelvis (Kerr's kink)
- fistulae

Ureteral TB

Complications

- **fibrosis & stricture formation**
  - **UVJ most commonly involved } usually intramural portion**
  - rarely involves UPJ **(UPJO)**
  - never middle third of ureter
- **VUR**

Bladder TB

Complications

- bullous granulations, ***TB ulcers*** (rare late finding), **tubercles** (rare, usually around UO)
- **usually starts around UO } "golf-hole" UO**
- Whole bladder covered by velvety granulations with ulcers
- healed ulcers have a stellate appearance
- bladder wall fibrosis & contraction } **"thimble bladder"**

TB of the genitals

C/P and complications:

- scrotal swelling: painful, inflamed (DD acute epididymo-orchitis)
- hematospermia
- Painless mass (r/o testis Ca)
- testicular involvement 2^{ry} to infection of epididymis
- infertility due to scarring & obstruction of epididymis or vas

TB of the prostate

- uncommonoften found in **TURP specimen**
- in rare, fulminating cases, disease spreads rapidly and can lead to a ***perineal sinus***.

TB of the penis & urethra

- uncommon
- superficial **ulcer** of glans (DD penile Ca)
- a **solid nodule** or as cavernositis with ulceration (rare)
- in active phase, urethral TB presents with *discharge*
- *urethral strictures*

Inv. **of GU TB**

- PPD skin test
- Lab.:
    - sputum for AFB
    - U/A, urine C&S(need special Lowenstein-Jensen medium)
    - routine bloods including creatinine and Ca (especially if calcifications)
- Rad.:
    - CT urography
    - CXR

- PPD TB test: (Purified Ptn. Derivative = Tuberculin test)
  - definition of a positive test:
    1) reaction of ≥5mm of induration: with
       - HIV +ve pts, recent contacts of TB cases.
       - fibrotic changes on CXR consistent with prior TB
       - Organ Tx and other immunosuppressed pts
    3) reaction of ≥10mm of induration in:
       - recent immigrants (<5yrs) from high-risk countries
       - **residents/employees of hospitals**, NHs, RHs, jails, etc
       - TB lab personnel
       - iv drug users
       - kids <4yrs of age or if exposed to adults at high risk
       - other high risk patients (DM, silicosis, CRF, head and neck Ca, gastrectomy, leukemias, jejunoileal bypass, etc)
    4) reaction ≥ 15mm of induration in persons with no TB RFs
  - significance of a +ve test:
    - evidence of infection
    - **no indication as to whether active or latent disease**
    - can't be sure that it's M. *tuberculosis* but it is far more common than nontuberculous Mycobacterial disease

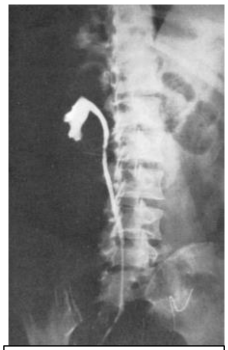
    → after a +ve PPD TB test, proceed to other inv.s

- Lab.:
  - urinalysis } RBCs, leukocytes, pH
  - urine C&S
    - takes 6-8weeks because M. *tuberculosis* is slow growing
    - Often negative so need **3-5 morning cultures**
    - culture on **Lowenstein-Jensen medium to isolate M. *tuberculosis***

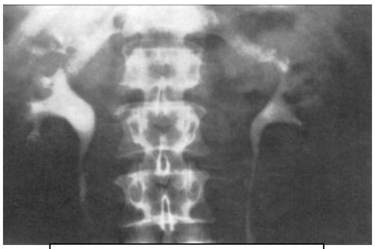
    N.B: urine AFB smears are often negative so not helpful

- Rad.
  - CXR } r/o old or active pulmonary TB
  - spinal xrays } r/o spinal TB (Potts)
  - KUB
    - renal calcifications, ureteral calcifications (rare)
    - calcification of bladder and SVs rare(in advanced disease)

  - IVP
    - Largely replaced by CT
    - **IVP findings of GU TB:**



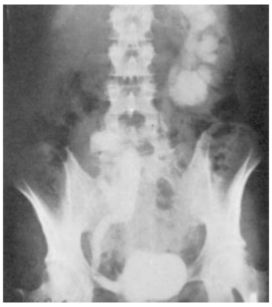
Occluded calyx



Distorted calyces

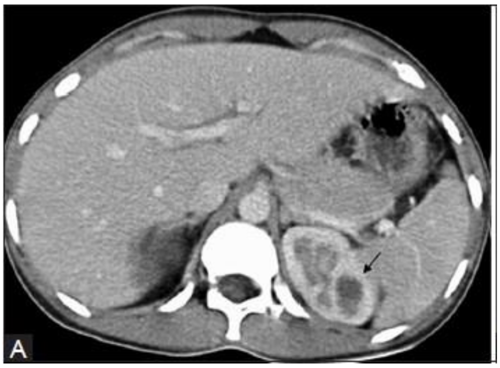
- Kidney
  - **small, non-functioning kidney w/ nephrocalcinosis (autoNx)**
  - **"moth-eaten" calyx (earliest sign – from papillary necrosis)**
  - **obliterated/occluded calyx.**
  - **infundibular stenosis.**
  - caliectasis.
  - calyceal or parenchymal destruction.
  - **renal calcifications.**
  - Kerr's kink (hiked up pelvis) رفع

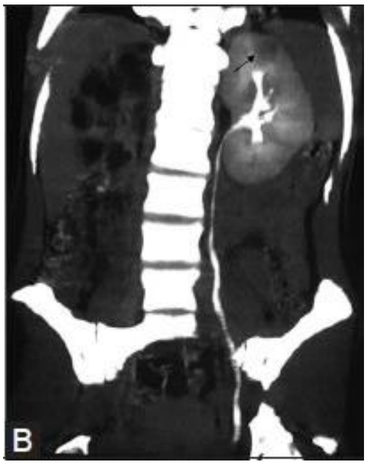
- Ureter
  - **ureteral dilation above a UVJ stricture**
  - rigid fibrotic ureter
  - **multiple ureteric strictures**
  - filling defects and ureteric calcifications (intraluminal)



Thimble bladder with R VUR

- Bladder/Urethra
  - **"thimble" bladder (small & contracted)**
  - **bladder calcifications**
  - SV calcifications (intraluminal)
  - fistulae } "watering can" perineum





كل الحاجات ممكن تتقال هنا

- **CT urography (equivalent to IVP)**
  - **identify extrapulmonary TB**
  - **CT findings of GU TB**:
    - **parenchymal scarring (most common finding – 80%)**
    - nephrocalcinosis
    - hydronephrosis or hydroureter (70%)
    - thickened walls of collecting system (60%)
    - hydrocalycosis, infudibular stenosis, UVJO or UPJO
    - string-of-pearls ureter
    - bladder filling defects
- **retrograde pyelogram**
  - characterize lower ureteric strictures
  - also for directed cultures (which side infected)
- **percuntaneous nephrostogram**
  - if retrograde access not possible to decompress obstructed system

- **cystoscopy +/- Bx**
  - rarely indicated in Dx of GU TB
  - Bx to r/o malignancy

ttt:

Medical Treatment

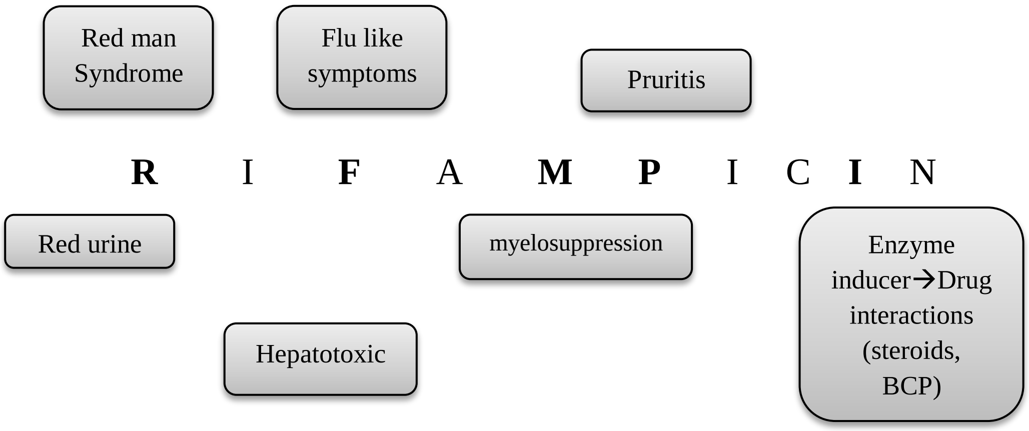
1st LINE

1) **Isoniazid (INH)**

- Dose: 300mg OD
- Mech.: inhibits synthesis of mycolic acids in M. *tuberculosis* by affecting enzyme **mycolase synthetase**
- Excretion
    - 70% excreted by kidneys but NO RENAL DOSING required
    - hepatic dosing recommended
- **Side effects:**
    - **hepatotoxicity** in 10-20%
    - **peripheral neuropathy** d.t. enhanced excretion of Vit B6 (give **vitamin B6 (pyridoxine)** supplements
    - SLE

2) **Rifampin**

- Dose: 600mg OD
- Mech.:
    - Abx isolated from ***Streptomyces mediterranei***
    - inhibits **bacterial RNA synthesis (bactericidal)**
- Excretion:
    - excreted in urine but NO RENAL DOSING required
- Side effects:



3) **Pyrazinamide**

- Dose *2g od*
- Mech.
  - inhibits **fatty acid synthetase I** of M. *tuberculosis* **(bactericidal)**
- Side effects:
  - **N/V** common
  - **interstitial nephritis** and
  - **thrombocytopenia**
  - **hepatotoxicity, arthralgia, hyperuricemia**

4) **Ethambutol**

- Dose: 15mg/kg OD or 1 gm OD
- Mech.
  - inhibits **cell wall synthesis (bacterostatic)**
- Excretion:
  - 80% excreted in urine needs **RENAL DOSING**
- Side effects:
  - can cause **hepatotoxicity,**
  - **retrobulbar optic neuritis** (need routine **visual acuity** checks and **red-green color** checks)

2nd LINE

5) streptomycin

- Dose: 1g OD
- Mech.
  - aminoglycoside isolated from ***Streptomyces griseus***

    - interferes w/ protein synthesis by binding to **30s unit of ribosome (bacterocidal)**
    - not active against intracellular mycobacteria
- Side effects:
    - **ototoxic** (reversible if stopped early after symptoms),
    - **nephrotoxic**

6) cycloserine

- Side effects
    - seizures, psychiatric disturbances

7) ciprofloxacin – Dose: 1.5g OD

8) ethionamide – Side effects: GI toxicity, hepatotoxicity, hypoT4)

➢ **Strategy of ttt**:

- ♥ **key is multi-drug Rx**
    - decreases duration of Rx &
    - reduces likelihood of drug-resistance
- ♥ **GU TB treatment**

INH + rifampin + pyrazinamide + ethambutol + Vit B6

For 6months

- ♥ give all meds in one dose qHS
- ♥ longer duration if disseminated TB, TB osteomyelitis, and TB meningitis

➢ Multi-drug resistant (MDR) TB:

- RFs:
    - prior Rx
    - living in country with high MDR TB rates (India, Russia)
- Rx 18-24 months } based on sensitivities

Surgical ttt

Adjuvant to medical Rx for GU TB.

- **If surgery necessary, delay until administration of meds for at least 4-6 weeks.**

➢ **surgical options for GU TB:**

  - aim: organ preservation & reconstruction not just excision

1) Nephrectomy

- extensive disease involving entire kidney + HTN + UPJO
- co-existing RCC
- symptomatic non-functioning kidney

2) Partial Nx

- **rarely indicated** } meds usually control local lesions (hard to justify w/o calcification)
- indications include:
    - localized polar lesion w/ calcifications that fails to respond to 6wks of meds
    - area of calcification that slowly increases in size, threatening entire kidney

3) Abscess drainage

- can all be done percutaneously } no need for open drainage with current imaging

4) **Epididymectomy**

- indications include:
    - caseating abscess that is not responding to meds
    - firm swelling that is slowly growing in size despite meds

5) Orchiectomy:

- testicular atrophy can occur in ~5%
- involvement of testis uncommon and orchiectomy (required ~5%)

6) management of ureteral strictures secondary to TB

- **UVJ most common site**
- distal ureter involved in ~10%
- recurrence is common, so careful f/u is required
- **Emergency management**
  - **Double J stent** or **NT** for drainage of kidney
- Medical tt:
  - start meds, steroids
- **Surgical repair of stricture: (**if deterioration or no improvement after ~3wks)
  - if deterioration or no improvement after 6wks,
  - method of repair
    - Surgical repair (depends on location & degree of stricture)

      Reimplant, Psoas hitch, Boari, etc
    - endoscopic treatment (lower success rates)

7) Augmentation cystoplasty: If:

1) intolerable frequency + pain, urgency, and hematuria
2) capacity <100cc
3) deterioration of renal function

- can use ileum, stomach, or colon
- inflammation of bladder not contraindication

8) Urinary conduit diversion: (with ileum or colon) If:

1) hx of psychiatric illness or mental retardation.
2) enuresis not related to small bladder capacity.
3) intolerable diurnal symptoms with incontinence.

PARASITIC INFECTIONS

- Schistosomiasis
- Filariasis (Wucheria branchrofti)
- Renal Hydatid disease (Echinococcosis granulosis)
- African river blindness (Onchocerca volvulus).
- Pelvic Enterobiasis (Entrobius vermicularis).
- Amebiasis (E. histolytica)

Schistosomiasis

Def.:

- Chronic disease caused by schistosomes, a genus of digenetic **parasitic trematodes.**

Pathogenesis:

- **Granulomatous host response to schistosome eggs** (T -cell dependent)

- Causative organism:
  - ***S. haematobium***
    - responsible for GU schistosomiasis
    - **Eggs with terminal spines (others have lateral spines).**
    - common in Middle East and Africa (Lake Malawi)
  - *S. mansoni and S. japonicum*
    - Disease in other parts of body (as the GI tract).

- **Life cycle of S. *haematobium*:**
  - **Miracidia** in Lake Malawi enters Snail and becomes **S**porocysts, then release into water as **Cercariae**,
  - then enter humans & become **Schistosomulum**

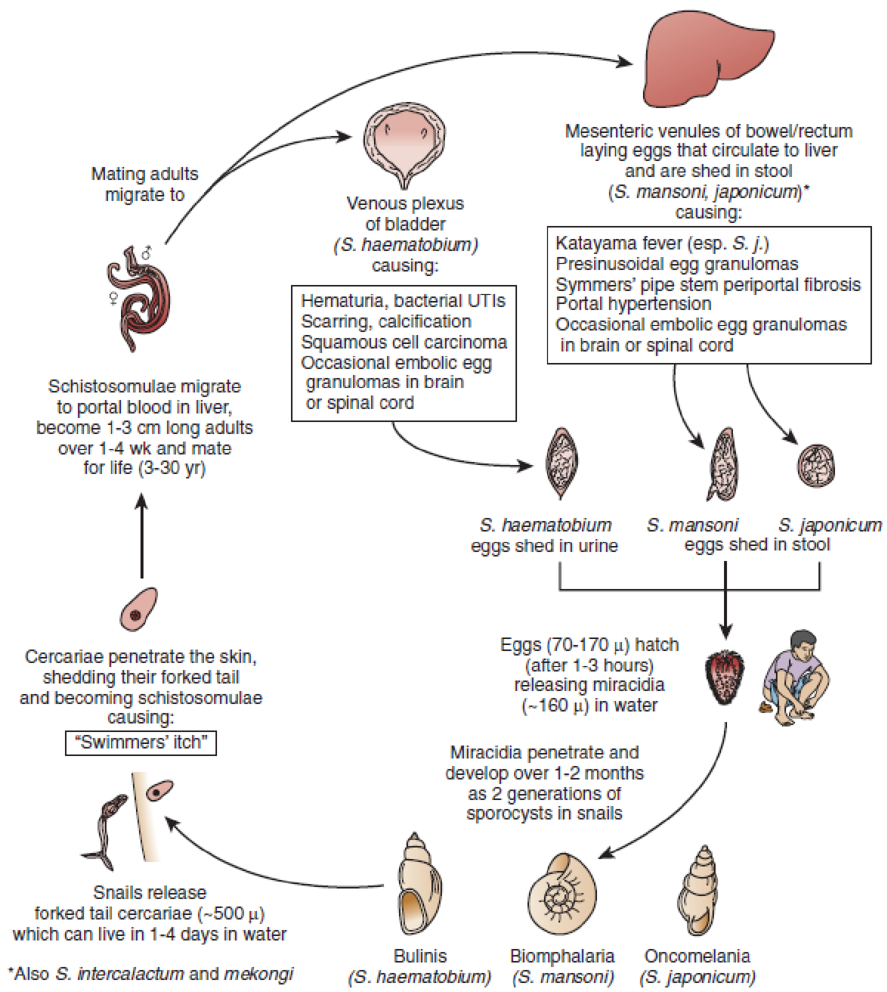
1) asexual reproduction

- **Miracidia** enters **snail** of *Bulinus* species → **sporocysts.**
- sporocysts → 20-40 daughter sporocysts (each → 200-400 **cercariae**) → **fresh water**
- **cercariae** penetrate skin of humans and sheds its tail to become **a schistosomulum.** (if cercariae don't penetrate skin → die within a few hrs)
- **schistosomulum** congregate in **lung** for 4-7 days, **in liver** from 2nd week onward
  - **adult worms** do not produce significant disease in host.
  - adults pair off and go to different sites to lay eggs.

2) Sexual reproduction

- **Adult worm** (1.5cm) **resides in vesical & pelvic venules.**
- M & F worms pair and attach to endothelium of blood vs.
- **lays eggs in venules**
  - 20% of eggs in hollow viscera excreted to urine or feces.
  - some eggs can travel in bloodstream to lungs, liver, etc
  - rest of eggs remain entrapped → calcified and accumulate
- estimated life span of worm is **3-6yrs**
- **egg** matures for several days until the **miracidium forms**
  - if not released into water → die and egg degenerates
- if miracidia exposed to water (urine or feces) then they migrate in fresh water to penetrate snail.

- in active infection, all egg stages are seen
- in cured or inactive infection, only degenerated (dark) or calcified eggs are seen



Life cycle of a schistosome

➢ Pathology:

1) active urinary schistosomiasis

- **viable adult worm pairs**, sustained egg laying,
- severe **periovial granulomas** (filled with viable eggs)
- bulky hyperemic **polypoid masses** projecting into lumen

2) inactive urinary schistosomiasis

- Dead adults worms (no viable worms in tissue/urine).
- Presence of **sandy patches:**
    - flat, tan mucosal lesions of various depth.
    - made of calcified eggs in dense fibrous tissue matrix.
- **calcified bladder on x-ray ("Baby's head")**

C/P:

1) **swimmer's itch (schistosomal dermatitis)**

- **pruritic rash** at site of cercarial penetration (after 3-18 hrs).

2) **acute schistosomiasis (*aka* Katayama fever)**

- fever, lymphadenopathy, splenomegaly, eosinophilia, urticaria & other manifestations of serum sickness-like disease(after 3-9 ws).
- more common with *S. japonicum* } rare with *S. haematobium*

3) **Chronic urinary schistosomiasis** (more common than acute disease):

a) **Chronic active phase**

- eggs deposited in tissue, traverse bladder and excreted → **hematuria + terminal dysuria**
- quiescent period } sx decrease, egg deposition occurs at lower rate
- **silent obstructive uropathy occurs** → hydroureteronephrosis
- **calcifications throughout collecting system**
- chronic/recurrent UTI w/ Salmonella → intermittent fever, anemia, splenomegaly
- nephrotic syndrome

b) **Chronic inactive phase:**

- viable eggs no longer detected in urine
- **"sandy patches" present** } flat mucosal lesions
- fibrosis & symptoms due to obstructive uropathy
- **calcified bladder ("fetal head").**

Diagnosis:

History → "Where have you been?"

Inv.:

- Lab.:
    - urine } presence of **terminally spined eggs**
      (egg excretion peaks b/w 10am-2pm**).**
- Rad.:

  (most important in chronic inactive schistosomiasis).

    - Xray
        - calcified bladder (looks like fetal head),
        - striations in ureters and renal pelvis

          N.B: ureteral calcifications are mural (unlike TB – forms cast of nondilated ureter)
    - IVP
        - hydroureteronephrosis, nonfunctioning kidney, tortuous ureters, ureteral stenosis, bladder & ureteral filling defects, mural calcification
    - VCUG
        - VUR (25%)
    - US
        - thickening of bladder wall, polypoid lesions of GU tract, hydro, calcific sandy patches
    - CT
        - obstructive uropathy and calcific lesions
- **rectal or bladder mucosal bx** } eggs seen on squash prep
- serologic testing

ttt:

Medical ttt

1) **praziquantel (drug of choice -** all schistosomal species)

- R/ Belicide, Biltricide, Distocide, Epiquantil, Praziquantel (600mg)
- Dose: 40mg/kg PO x 2 doses
- Mech.: interferes w/ ion transport in schistosome.
- S/E's: GI complaints, h/a, dizziness, fever

2) oxamniquine

- effective only against *S. mansoni*
- given over 2-3 days

N.B:

- R/ Mirazid 300mg (commiphora ext.) used for cestodes.
- **no effective prophylactic drug (**avoid infected streams, rivers, lakes)

Surgical ttt

Always treat with meds first

- **Indications:**

1. complications not responding to med ttt (eg obstructive uropathy)
2. intractable bladder hemorrhage

Prognosis:

- generally good esp. with newer drugs (pts that die are usually young, early stage disease, heavy total egg burden).
- poor prognosis w/ bacterial superinfection
- transplant donor/recipient not contraindicated } need 2 months of chemo prior

Complications:

✚ **anatomic GU Complications of *S. haematobium*.**

1) Kidney and Ureter

- ureteritis cystica calcinosa
- **stones**
- **hydroureteronephrosis (obstruction and ureteral hypotonia)**
    - hydroureter before hydronephrosis (final stage).
- ureteral obstruction
    - Sites:
        - UO, interstitial, juxtavesical and/or lower 1/3 ureter
    - causes
        - concentric polypoid lesions
        - eggs perforate urothelium (urine→ interstitium →spasm)
        - ureteral hypotonia
    - Rx: ureteric Sx if residual disease after meds
- **Renal failure**
    - **d.t SOU – schistosomal obstructive uropathy.**
    - **most common sequelae of GU schistosomiasis**
- XGP

2) Bladder

- polyposis
- **sandy patches**
- **"contracted bladder" syndrome.**

    - occurs in later chronic active stage (highest egg burden)

    - get constant deep lower abdo/pelvic pain, LUTS, UI

- ulceration
    - 2 types } **acute** (necrotic polyp sloughs) or **chronic**.
    - occurs at posterior midsagittal line middle to upper.
    - Rx → chronic deep bladder ulcers requires partial cystectomy (not fulguration).

- hyperplasia/metaplasia
    - squamous or adenomatoid differentiation
    - epidermization.
- cancer
    - **SCC (60-90%) and adenocarcinoma**
    - early onset (40-50 yrs),
    - SOU predisposes to UTI (bacteria produce carcinogenic nitrosamines)
    - Site: usually on posterior or lateral wall
    - C/P: nocturia, pain, hemorrhage
    - Rx: Radical anterior exenteration w/ urinary diversion
- UO obstruction
- UTI (recurrent UTI from *Salmonella)*

3) Urethra, Prostate, SV, BOO, Genitals

- cervical stenosis, cervicitis & vaginitis (dyspareunia common)
- asymptomatic hematospermia
- eggs/blood in ejaculate

Anatomic non-GU complications of *S. Haematobium:*

- GI tract
    - sandy patches in rectum.
    - schistosomal colonic polyposis:
        - abdo pain, dysentery, finger clubbing, arthralgia, anemia, protein-losing enteropathy
        - requires cross-infection w/ *S. haematobium* and *S. mansoni*
    - schistosomal appendicitis.
- pulmonary involvement
- CNS involvement
    - space-occupying lesion, myelitis, transverse myelitis
- bilharziomas

N.B **No documented case of fetal schistosomiasis**

Filariasis

Prevalence:

- distributed in tropics and subtropic areas

Pathogenesis:

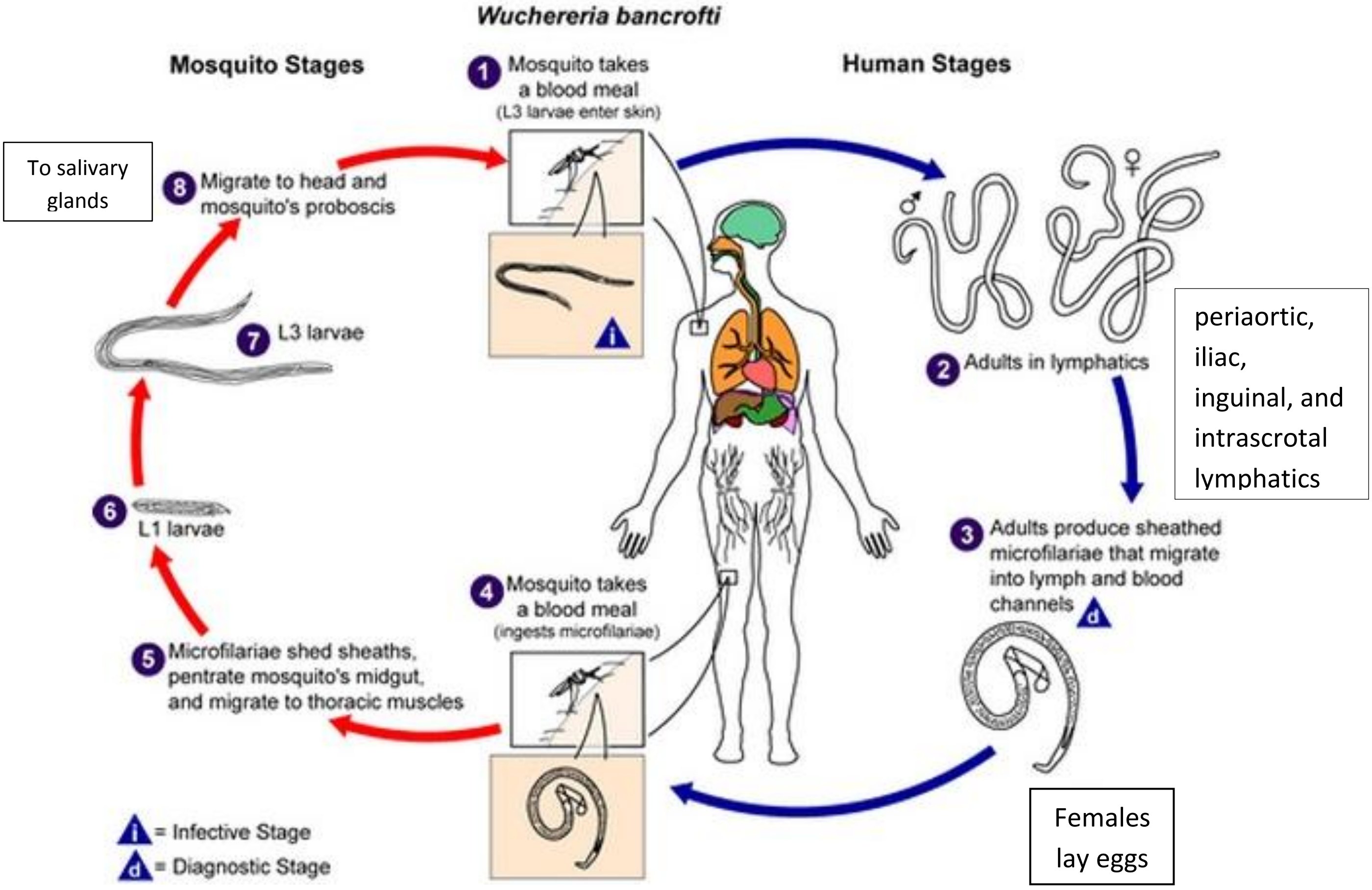
- Causative organism in genital filariasis:
  1) Lymphatic filariasis
     - ***Wucheria bancrofti***
       - **causes 90% of lymphatic filariasis in humans**
     - *Brugia malayi & Brugia timori.*

2) Non-lymphatic filariasis

- *Loa*
- *Dietalonema, Dirofilaria, Mansonella*
- *Onchocerca volvulus*: causes scrotal elephantiasis, African river blindness.

- **life cycle of the lymphatic filariae.**

  cycle proceeds from **human to mosquito and back**


Wuchereria bancrofti
Mosquito Stages
Human Stages
1 Mosquito takes a blood meal (L3 larvae enter skin)
2 Adults in lymphatics
♂
♀
3 Adults produce sheathed microfilariae that migrate into lymph and blood channels
4 Mosquito takes a blood meal (ingests microfilariae)
5 Microfilariae shed sheaths, pentrate mosquito's midgut, and migrate to thoracic muscles
6 L1 larvae
7 L3 larvae
8 Migrate to head and mosquito's proboscis
i
d
i = Infective Stage
d = Diagnostic Stage

To salivary glands

periaortic, iliac, inguinal, and intrascrotal lymphatics

Females lay eggs

- Pathogenesis of lymphatic filariasis.
  1) Prepatent period
      - **lymph vessels harbour worms → dilated**
      - edema, vasodilation, inflammatory infiltration of tissues drained by lymphatics.
  2) Early established infection
      - **lesions persist and cause significant scarring**
      - lesions at worms' nesting areas } **epididymitis, orchitis, filarial lymphangitis, filarial abscess**
          - worm death causes inflammatory response
          - exudative filarial lesions simulate abscesses → sterile
  3) Late infection
      - **lymph vessels obstructed**
      - huge hydroceles and scrotal, penile elephantiasis (elephant scrotum often becomes secondarily infected, BUT hydroceles don't)
- C/P of lymphatic filariasis:
- ✓ asymptomatic
  - skin test reactivity only
- ✓ filarial fevers
  - episodic fevers, lymphangitis, epididymitis, small hydroceles, chronic hydrocele, chyluria, lymph scrotum
  - typically amicrofilaremic
- ✓ tropical eosinophilia (peripheral eosinophilia, responds to antifilarial drugs)
- ✓ Chronic lesions
  - **funiculoepididymitis**
    - pain, lumpy or cordlike swelling, hydrocele with varicocele or thrombosis of pampiniform plexus
    - Rx (ABx, surgical decompression, excision of filarial nodules, orchiectomy)
    - orchitis is rare, sterility is rare

- **hydrocele**
  - thick fibrous tunica w/ cholesterol or Ca deposits
    - calcification rare in hydrocele (presence suggests infectious/filariasis)
  - milky or sediment-rich hydrocele fluid
- **scrotal and penile elephantiasis and lymph scrotum**
  - skin ulcers and sepsis (Rx excision w/ grafting)
- **chyluria**
  - dying worms cause lymphatic obstruction.
  - rupture of lymphatic varix into collecting system.
  - severe protein loss, hypoalbuminemia, anasarca.

Dx of filariasis:

1) **histologic finding of adult worms**
2) *Brugia* or *Wucheria* in blood, chylous urine, or hydrocele fluid } peak microfilaremia at midnight
3) U/S observation of worms } "filarial dance sign"

ttt:

Medical management

1) **diethylcarbamazine (DEC) (gold standard) R/ Hetrazan 5o mg**

- **Dose: 2 mg/kg/day PO TID x 2 weeks** (prophylactic 6mg/kg/year**)**
- S/E's } fever, N/V, arthralgias (due to dying filariae)

2) ivermectin R/ **Ivactin 6 mg**

- Dose: single dose 200-400 ug/kg
- no effect on adult filariae

3) **albendazole** R/ **Vermizole 200mg**

- kills both adults and microfilariae

4) elastic stockings & elevation of extremities

5) lymphangiogram + sclerosis of lymphatic fistulae

Renal Echinococcosis

Def.

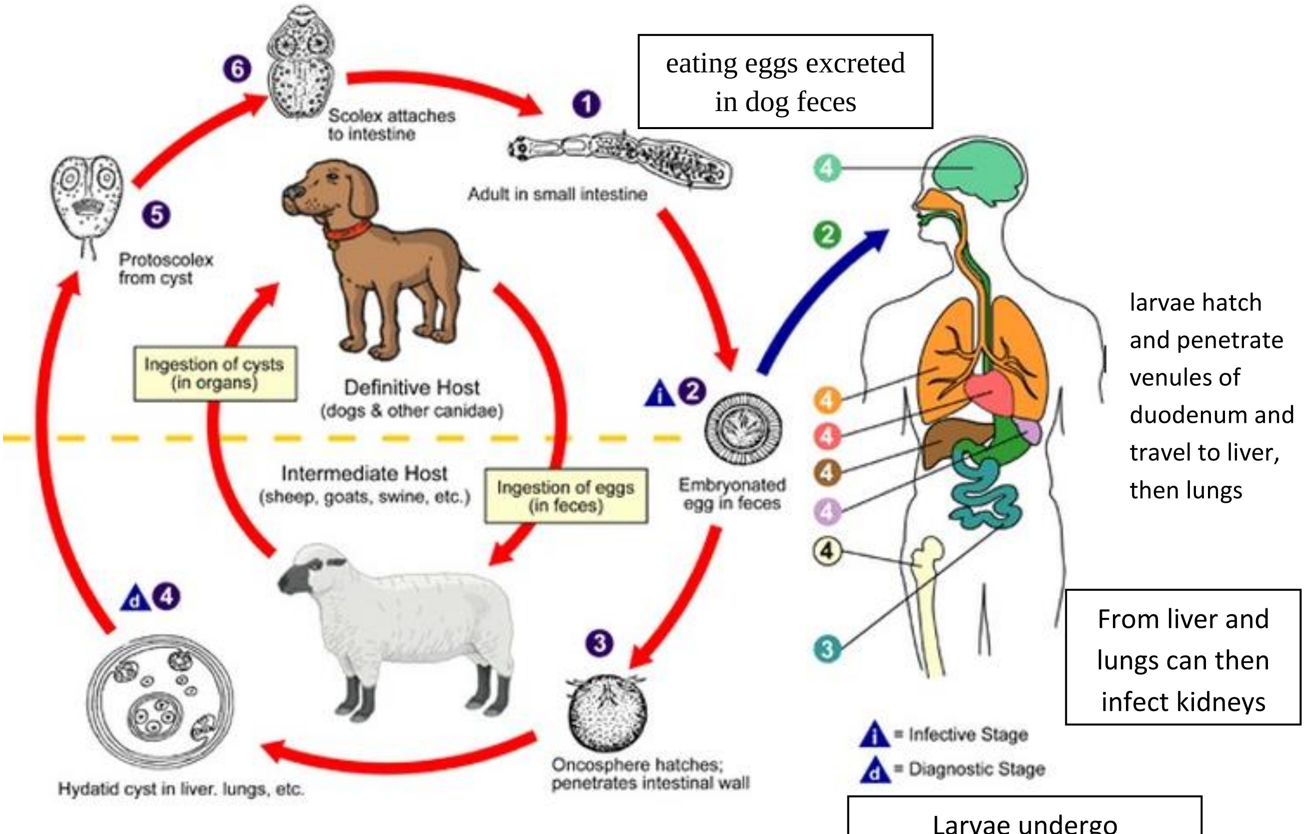
- larval stage of tapeworm **Echinococcus granulosus**

Incidence:

- seen in dogs, sheep, cattle
- seen in humans in S. Africa, Australia, Mediterranean countries
- **Any organ or body part can be involved with hydatid cysts (**Renal hydatids ~2% of hydatid disease)

Pathogenesis:

➢ life cycle:


6
Scolex attaches to intestine
1
Adult in small intestine
5
Protoscolex from cyst
Ingestion of cysts (in organs)
Definitive Host (dogs & other canidae)
i 2
Embryonated egg in feces
Intermediate Host (sheep, goats, swine, etc.)
Ingestion of eggs (in feces)
d 4
3
Hydatid cyst in liver, lungs, etc.
Oncosphere hatches; penetrates intestinal wall
4
2
4
4
4
4
4
3
i = Infective Stage
d = Diagnostic Stage

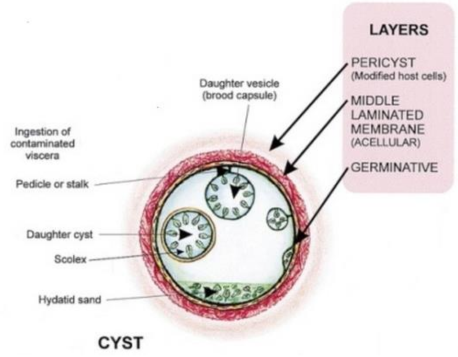
eating eggs excreted in dog feces

larvae hatch and penetrate venules of duodenum and travel to liver, then lungs

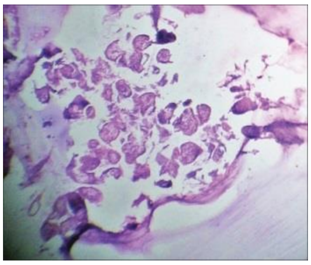
From liver and lungs can then infect kidneys

Larvae undergo vesiculation → hydatid cyst (grows at 1cm/yr)

- definitive host } dog
- intermediate host } sheep



- Pathology:
  - Shape of renal cysts:
    - usually single and located in the cortex
    - hydatid cyst has 3 zones;
      - peripheral zone } **fibroblasts** that may calcify
      - intermediate layer } **laminated layer** becomes **hyalinized**
      - inner layer } The **Germinal epithelium**
    - **New larvae** develop in germinal layer within **brood capsules**.
    - detached brood capsules called **daughter cysts**
    - **hydatid sand** = free larvae + daughter cysts.
  - cyst contents are highly antigenic } risk of fatal anaphylaxis



C/P:

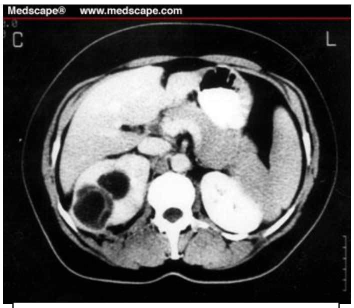
- **most are asymptomatic**
- Presents as slow growing tumour (flank mass, dull pain, and hematuria).
- cyst is focal and so DOES NOT cause renal failure
- if cyst ruptures into collecting system,
  - pt may have renal colic from passage of debris → **hydatiduria** (resembles grape skins).
  - daughter cysts in urine; may see laminated wall of cyst.

Inv.:

- Lab.:
  - may see eosinophilia
  - Urine analysis:
    - daughter cells in urine
    - laminated wall of cyst in urine
    - microscopic hematuria (rare)

- **+ve double-diffusion test**
    - using partially purified hydatid arc 5 antigens
- serologic testing: complement fixation, HA, and Casoni intradermal skin tests are less reliable

- Rad.:
    - IVP
        - thick-walled cystic mass, occasionally calcified
        - if cyst ruptures → daughter cysts outlined in renal pelvis
    - ultrasound
        - multicystic or multiloculated mass
        - **movement** shows bright falling echoes within (hydatid sand)
    - CT
        - cystic mass w/ discrete, round daughter cysts & well-defined enhancing membrane
        - may also present as thick-walled multiloculated cystic mass (less specific)



Hydatid membrane with scolices

DDx

- simple cyst
- renal abscesses
- infected cysts
- necrotic RCC

N.B **Daughter cysts within mother cyst differentiates renal echinococcosis**

ttt:

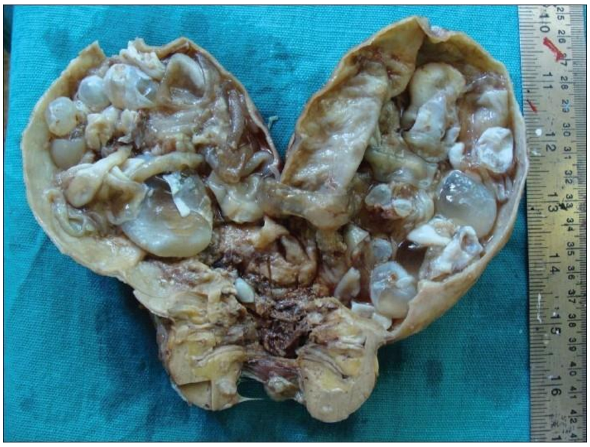
DO NOT FNA→ ruptures cyst and releases highly antigenic contents (anaphylactoid rxn)

- prognosis is good but depends on site and size of cysts

1) medical therapy:
    - **albendazole** 400mg PO BID x 1-6 months
    - **praziquantel** preoperatively
    - mebendazole → limited success with significant S/Es

2) surgery } **mainstay of treatment**

- **removal of cyst without rupture** (reduce chance of seeding and recurrence)
- if wall is calcified, larvae are dead so low risk of seeding
- be careful of living daughter cells
- if cyst must be ruptured, aspirate first then instill into cyst some 2% formalin or 1% iodine



Isolated renal hydatid disease

Other GU Parasites

Onchocerca volvulus (causes **African river blindness**)

- transmitted by black flies of *Simulium* species
- C/P: blindness, atrophic dermatitis, scrotal elephantiasis
- Rx Ivermectin +/- doxycycline (6 weeks course)
  - don’t use DEC d.t severe allergic immune responses to dying microfilariae (Mazzotti reaction)

Enterobius vermicularis:

- common intestinal pinworm
- can cause **pelvic enterobiasis** (anus → vagina→ peritoneal cavity)
- Rx Pyrantel, pamoate, mebendazole, or albendazole

E. histolytica: (**amebiasis)**

- rare cause of renal abscess } R kidney more common
- usually accompanied by liver abscess
- C/P: hematuria, amebic ulceration of perineum
- Rx metronidazole ASAP

Trichomonas vaginalis **(Trichomoniasis**)

Plasmodium falciparum (**Malaria**)

Strongyloides stercoralis (**Strongyloidiasis)**

- fourth most important intestinal nematode infection in the world
- Rare GU infection

Gnathostoma spinigerum **(Gnathostomiasis)**

- consumption of raw or undercooked infected fish
- superficial subcutaneous manifestations, deeper visceral tissues (rare GU cases).
- Ttt: treatment is surgical excision when possible + Albendazole

FUNGAL INFECTIONS

Classification of fungal infections of the GU system:

1) Opportunistic fungi

- **Candida } most common**
- *Torulopsis glabrata*
- Aspergillosis
- Cryptococcosis
- Phycomycosis (Mucormycosis, Zygomycosis)

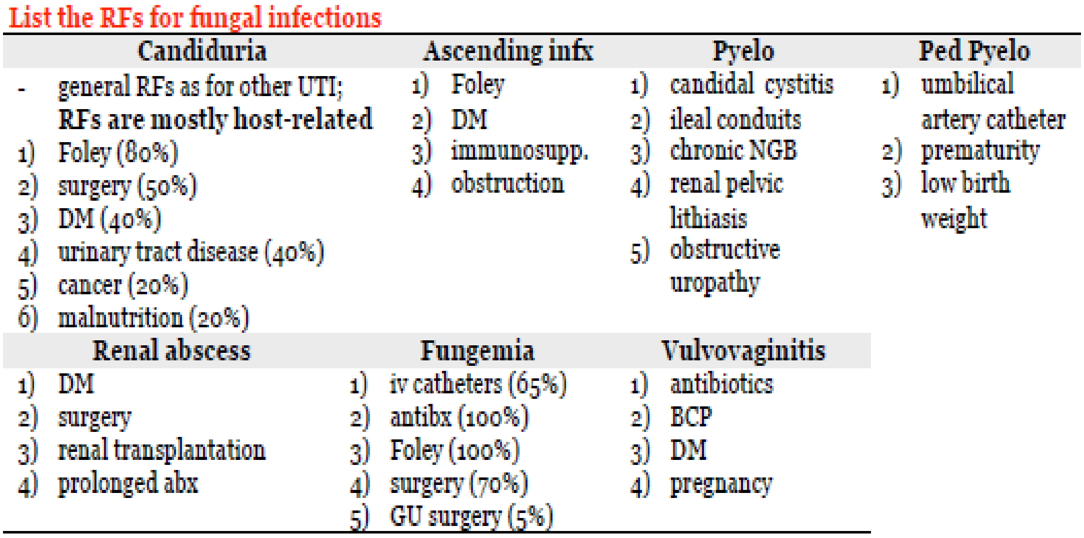
2) Primary fungal infections

- Blastomycosis
- Coccidiomycosis
- Histoplasmosis

3) Rare and unusual

- Phaeohyphomycosis - *Pseudallescheria boydii*
- *Fusarium* - Rhinosporidiosis
- Paracoccidioidomycosis - Sporotrichosis
- Penicillium - Tinea
- Trichosporon

4) Actinomycetes



List the RFs for fungal infections

Candiduria	Ascending infx	Pyelo	Ped Pyelo
- general RFs as for other UTI; **RFs are mostly host-related** 1) Foley (80%) 2) surgery (50%) 3) DM (40%) 4) urinary tract disease (40%) 5) cancer (20%) 6) malnutrition (20%)	1) Foley 2) DM 3) immunosupp. 4) obstruction	1) candidal cystitis 2) ileal conduits 3) chronic NGB 4) renal pelvic lithiasis 5) obstructive uropathy	1) umbilical artery catheter 2) prematurity 3) low birth weight

Renal abscess	Fungemia	Vulvovaginitis
1) DM 2) surgery 3) renal transplantation 4) prolonged abx	1) iv catheters (65%) 2) antibx (100%) 3) Foley (100%) 4) surgery (70%) 5) GU surgery (5%)	1) antibiotics 2) BCP 3) DM 4) pregnancy

Candida

Species of Candida cause GU infections:

- ***C. albicans:* 74% *C. glabrata***: 8%
- *C. parapsilosis, C. tropicalis, C. lusitaniae*

Primary sites of candidemia infection:

- **Intravascular catheters (65%),** TPN
- GU tract (kidney most common), GI tract, respiratory tract

C/P

→ usually asymptomatic

- LUTS
- flank pain/renal colic } **fungus balls**
- pyelo symptoms } flank pain, renal tenderness, fever
- oliguria/anuria } due to obstruction
- recurrent fever in immunocompromised pt

C/P of candiduria (acc. To site):

1) superficial infection
- around ileostomies/cutaneous pyelostomies
- P.O wound infection (erythema and pustules in incision sites)
- Rx topical antifungals

2) vaginitis
    - yellowish-white vaginal **D/C** & gray-white pseudomembranous exudate in vagina + **pruritis**
    - Rx oral fluconazole (150mg od x1) or intravaginal Rx

3) genital infection
        - emphysematous cellulitis, epididymitis

4) bladder/prostate infection
    - emphysematous cystitis/prostatitis
    - **fungal bezoar**
    - **prostatic abscess**

5) upper tract infection
    - **fungus balls**: ureteral obstruction or renal pelvis obstruction
    - **perinephric abscess**
        - fever, flank pain,+ve culture for *Candida*, abn. US/CT
        - mainly in DM on prolonged ABx
    - candidal pyocalix, pyelonephritis, papillary necrosis

6) systemic candidal infection

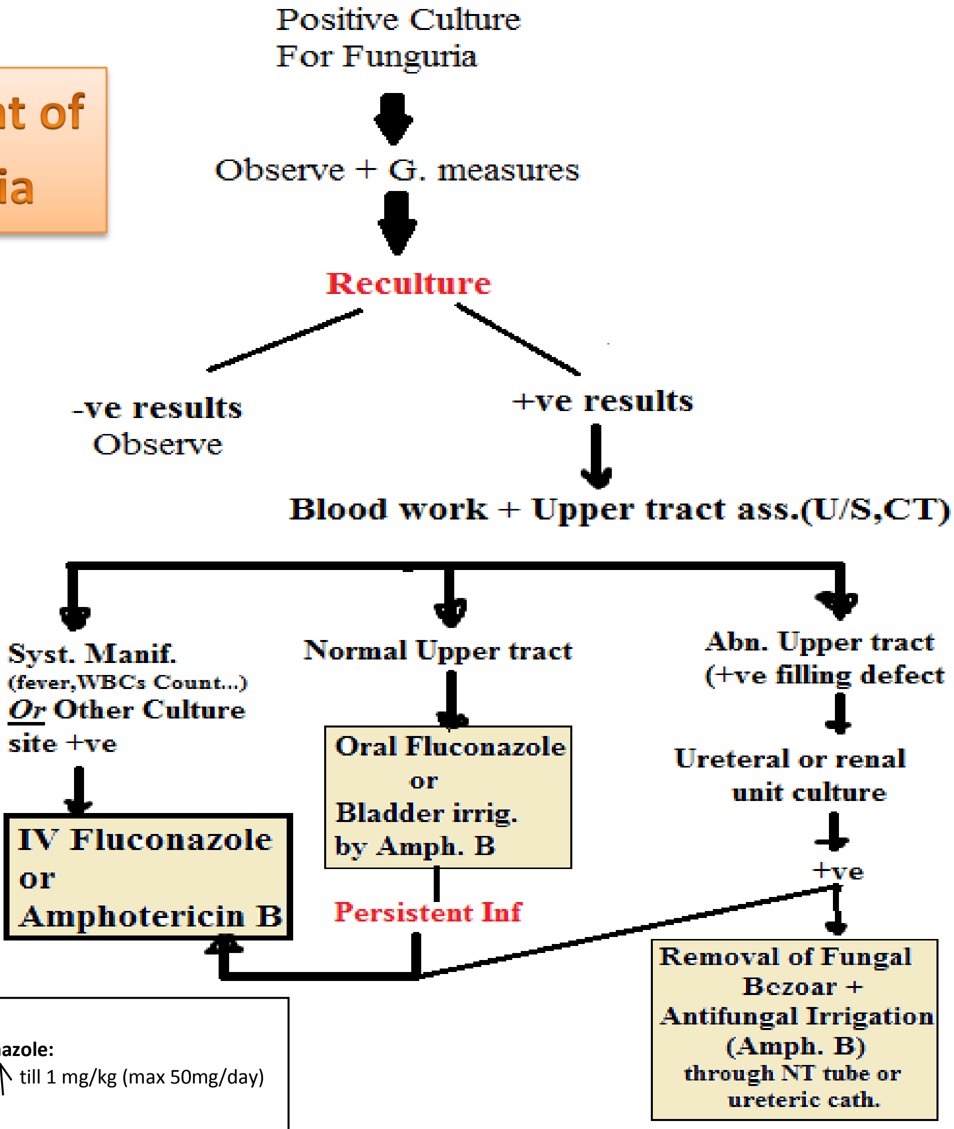
Inv.

- Detect fungus by:
    - **smear or culture of wound exudate** → superficial infection
    - **microscopic** or **culture** in vaginal exudates
    - cystoscopy → bladder
- Lab:
    - Urine studies
        - microscopic examination finding:
            - budding forms or pseudohyphae
            - pyuria and hematuria
            - fungal casts
        - culture from urine } **CLED agar** (cystine lactose electrolyte deficient), blood agar, and **Sabouraud's agar** w/ dextrose
        - urinary candidal colony counts } **high counts if renal infection vs. colonization**

→ **cannot be used to differentiate colonization from local or invasive infection, especially if indwelling catheter.**

- Blood/serologic studies (no lab studies can indicate upper tract inf.)
  - persistence of positive Candida blood cultures
  - antibody response to candidal antigen
  - PCR → for occult candidemia
- Rad.:
  - cystogram, IVP, retrograde } filling defects
  - US } demonstration of fungal material
  - CT } mass lesion w/ less attenuation than stone (detects obstructive uropathy)
- **Bladder cystoscopy**
  - white patches on bladder wall + areas of mucosal edema & erythema, and hyphae in exudates

Treatment of Funguria


Positive Culture For Funguria
Observe + G. measures
Reculture
-ve results Observe
+ve results
Blood work + Upper tract ass.(U/S,CT)
Syst. Manif. (fever,WBCs Count...) Or Other Culture site +ve
IV Fluconazole or Amphotericin B
Normal Upper tract
Oral Fluconazole or Bladder irrig. by Amph. B
Persistent Inf
Abn. Upper tract (+ve filling defect
Ureteral or renal unit culture
+ve
Removal of Fungal Bezoar + Antifungal Irrigation (Amph. B) through NT tube or ureteric cath.

Doses:
IV Amph. B or Fluconazole:
Start with 1 mg and ↑ till 1 mg/kg (max 50mg/day)
Oral Fluconazole:
200mg* 1d
100mg/d for 2 weeks
Bladder irrig. Amph. B
50mg/ 1 litre over 24 h

Treatment options for a GU candidal infection:

- observation
- general measures
  - removal of foreign bodies (catheters, IVs)
  - improve nutritional status
  - stop unnecessary antibacterial agents } restore N flora
  - relief of obstruction
  - urine alkalinization can decrease multiplication of fungal elements
- antifungals
  - Irrigation (amphotericin B or miconazole)

    ➔ **acidic urine decreases effectiveness**
  - Oral therapy
  - systemic Tx (amphotericin B or fluconazole) if:
    - local infection
    - invasive or disseminated infection
- surgical
  - } debridement
  - } removal of fungal ball
  - } correction of underlying abnormalities

indications for nephrectomy with fungal infection?

1) fungal abscess
2) cellulitis
3) diffuse parenchymal infection

Treatment plan:

(Treatment of only symptomatic funguria recommended)

1) Initial candiduria (single +ve culture)

- observation if urine colony counts <10000,
- Do general measures

2) Reculture

If –ve Observe

if +ve :

- assess for upper tract abnormalities } US, IVP, CT
- **if +ve filling defects**

  ➔ **perform culture ureteral/renal urine:**
    - if +ve:
  - **antifungal irrigation** w/ ampho B via NT or ureteral catheter
  - perc removal of fungal bezoar
  - **systemic ampho B (R/ Fungizone 50 mg), IV fluconazole (R/ Diflucan 50,100ml)**

    Dose: 1mg then increase by 5mg to ~0.5-1.0mg/kg (max 50mg/day.
- **If no upper tract abnormalities**
  - PO fluconazole for 2-3 weeks or
  - Bladder irrigation for 1 week
    - bladder irrigation not preferred any more
    - 50mg of amphotericin B in 1L sterile water over 24hrs

3) if systemic manifestations (fever, WBC, other culture sites +ve)

- **systemic ampho B, IV fluconazole**

4) if no systemic manifestations

- bladder irrigation w/ **ampho B (50mg in 1000cc water/D5W at 1L/day)**
- **PO/IV fluconazole**
- if persistent infection } **systemic ampho B, IV fluconazole**

- S/E's fluconazole:
  - **renal clearance** } renal dosing REQUIRED
  - N/V, abdo pain, diarrhea
  - **Rash**, rarely liver failure
  - increases effects of Coumadin
- S/E's iv amphotericin:
  - **Biliary clearance** (usually no renal dosing required) but **Bean toxicity (nephrotoxic**)
  - HypoK, HypoCa, HypoMg
  - Anemia, thrombocytopenia, Arrhythmias
  - **Myalgia/flu-like symptoms** (fever, chills, etc) - Ototoxicity
  - **Microcephaly (only congenital anomaly)**
  - Phlebitis, Anaphylaxis, Multi-organ failure (liver, etc)
- Specific infections:
  - Candidal vaginitis:
    - **PO fluconazole 150mgx1 (equals intravaginal clotrimazole)**
    - nystatin intravaginally x 14 days
    - boric acid powder
    - chronic infections } ketoconazole 400mg OD x 14d followed by 100mg OD x 6/12
  - Candidal infection of the upper tracts?
    - NT (relieves obstruction)
    - IV ampho B
    - irrigation of renal pelvis w/ ampho B
    - surgical drainage or Nx for perinephric abscess

N.B:

- fluconazole **treats all** species of Candida **except C. krusei and C. glabrata**
- **A**mphotericin B 6mg/kg **is the gold standard for treatment of the pt w/ invasive or disseminated fungal infection**

Aspergillus

- major cause of M&M in immunocompromised patients
- extra-pulmonary aspergillosis is uncommon
- most common species cause GU infection
  - *A. fumigatus* - *A. terreus* - *A. flavus* - *A. niger*
- **GU manifestations**
    - renal infection
      - renal aspergillomas/pseudotumours in AIDS pts
      - abscesses
      - fungal vascular occlusion } renal infarcts
    - prostatic infection and BOO
    - disseminated aspergillus
- Dx
  - urine/tissue biopsy } PAS stain of the fungus
  - blood cultures } usually –ve
  - PCR amplification
- **treatment of Aspergillus?**
  - **poor outcomes in invasive aspergillosis } mortality rates~40-90%**
  - Medical
    - } **amphotericin B (traditional drug of choice)**
    - } itraconazole

      Dose: IV amphotericin B 1.5g x 3weeks + PO itraconazole 200 mg PO BID x 3 months
  - Surgical
    - endourologic access (anterograde or retrograde)
    - irrigation (via NT or ureteral catheter)
    - lavage and debulking (PCNL or via ureteropyeloscopy)
    - re-irrigation
    - renal exploration, pyelotomy
    - nephrectomy

Cryptococcosis

- *Cryptococcus neoformans*.
- often self-limiting
- **usually an asymptomatic pulmonary infection**
- CNS is primary target of hematogenous spread
- DX
  - identification in urine, CSF, or others }Sabouraud's glucose agar
  - cryptococcal antigen in urine of AIDS pts
- **GU manifestations of Cryptococcal infection?**
  - Renal and adrenal infection (cryptococcal pyelo)
    - Rx amphotericin B
  - Prostatic infection
    - Rx requires systemic fluconazole
  - Genital infection → epididymitis
    - Rx orchiectomy + systemic ampho B, ketoconazole, fluconazole
  - Penile infection } glans ulcer to large exophytic lesion
    - Rx excisional Bx and systemic Rx (ampho B or fluconazole)

Mucormycosis (Phycomycosis)

- **renal involvement } high mortality rate if untreated**
- **Nx + systemic amphotericin B } ~75% survival**

Blastomycoses

- *Blastomycoses dermatitidis*
- ***Local*** : Prostatitis and prostatic abscess, epididymitis (common), adrenal infection, Or ***Systemic*** blastomycosis
- Dx +ve Blastomyces skin test and Blastomyces A antigen
- Disseminated disease } systemic amphotericin B 1-3g
- Mild/moderate non-meningeal forms } ketoconazole 400mg OD

Coccidioidomycosis

- *Coccidioides immitis*
- **usually asymptomatic and transient pulmonary infection**
- "allergic" reaction to infection } erythema nodosum. aka **"valley bumps"** or **"valley fever"**
- **GU manifestations of coccidioidomycosis?**
    - Kidney, adrenal, prostate, bladder (coccidioidal cystitis), scrotal swelling
    - urethrocutaneous fistulae
- **similar to TB** } "moth-eaten" calyces, infundibular stenosis, renal calcification
- systemic antifungals } amphotericin B 1-1.5 mg/kg/d x 2-3mo
- surgical resection of infected scrotal contents or prostate

Histoplasmosis

- *Histoplasmosis capsulatum* **(major opportunistic infection in AIDS patients)**
- +ve histoplasmin skin tests
- **GU manifestations of histoplasmosis:**
    - adrenal (Addison's disease), renal, genital (superficial penile ulcers)
- systemic amphotericin B

Sporotrichosis

- induces chronic lymphocutaneous lesion

Actinomyces

- **Describe the urogenital manifestations of actinomyces infection.**
    - retroperitoneal abscess (renal infections, renal-colic fistula, renal duodenal fistula, intratesticular abscess, ureteral obstruction
- □ **Medical } penicillin IV 20 million units / day x 2 weeks**

Specific situations

Bacteriuria in Pregnancy

Definition of bacteriuria

- In a pregnant woman, asymptomatic bacteruria is diagnosed in case of **two consecutive** voided urine specimens with grow of > 10^5 cfu/mL of the same bacterial species; or a **single catheterised** specimen with grow of >10^5 cfu/mL of a uropathogen
- In a pregnant woman with symptoms compatible with UTI bacteriuria is considered relevant If a voided or catheterised urine specimen grows > 10^3 cfu/mL of a uropathogen

How common is bacteriuria during pregnancy?

- prevalence same as in non-pregnant women
- asymptomatic bacteriuria is most common infectious complication of pregnancy
- asymptomatic bacteriuria DOES NOT CLEAR spontaneously as frequently as in nonpregnant women → more symptomatic and tend to remain bacteriuric
- site of infection doesn't change with pregnancy
- more common later in pregnancy, in low SES, multiparous women, and women with sickle cell trait
- women w/ renal source of bacteriuria are more likely to have persistent postpartum bacteriuria

Incidence

- develops in 1-4% of all pregnant women } 20-40% of pregnant women w/ unRx'd bacteriuria
    - Most women → asymptomatic bacteriuria before pregnancy
    - 20-40% of women with asymptomatic bacteriuria → pyelonephritis during pregnancy
- ~75% get pyelo during T3 } when hydro and stasis in GU tract is greatest
- 1/3 of pregnant women that get pyelo have a prior hx of pyelo
- screening for bacteriuria decreases incidence of acute pyelo
- those with infections localized to kidney have increased evidence to suggest hx of chronic pyelo
- □ increased likelihood that bacteriuria progresses to acute pyelonephritis during pregnancy

GU changes during pregnancy:

- Renal
    1) ↑'d renal size } renal length increases approximately 1 cm
    2) ↑'d RBF
    4) ↑d GFR: 30-50%
    5) ↑'d protein excretion (normal up to 300mg/day)
    6) ↑'d urine Ca, citrate, and uric acid excretion
    7) ↓'d Cr and BUN
    8) ↑d susceptibility to pyelonephritis
    9) urine volume increases in upper tract

- Collecting system
    - hydronephrosis
        - more common on R } left side protected from compression by sigmoid
        - decreased peristalsis during pregnancy
        - most women in 3rd trimester show significant ureteral dilatation (90% in T3)
    - initially due to muscle-relaxing effects of increased progesterone
    - later due to mechanical compression by enlarging uterus

- Bladder & Urethra
    - bladder becomes hyperemic
    - bladder hypertrophy
    - squamous changes of the urethra } due to estrogen
    - SUI
    - storage LUTs

Complications

- higher incidence of pyelo & sepsis } ↑’d incidence of prematurity, low birth wt & fetal death
- slightly higher risk of developing anemia

Diagnosis of UTI in pregnant women

- similar to that of non-pregnant women
- physical examination and urinalysis including urine culture are highly recommended in cystitis.

- In addition, in case of suspicion of pyelonephbritis, ultrasound of the kidneys and urinary tract is necessary.

Recommendations for screening for bacteriuria?

- urinalysis + urine C&S during T1 } if negative, no need to test further as these patients are unlikely to develop bacteriuria later
- u/a alone has too high a false –ve rate
- if hx of recurrent UTIs or VUR, may benefit from Abx prophylaxis

ttt:

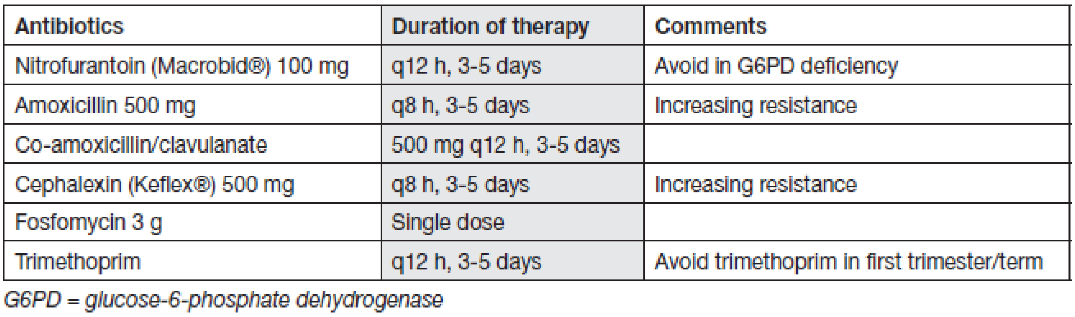
- ➢ pathogens similar to those seen in non-pregnant women
- ➢ must consider fetal toxicity
- ➢ full 3-7 day course recommended
- ➢ f/u cultures recommended
- ➢ if bacterial persistence or rapid reinfection consider Abx prophylaxis during pregnancy
- ➢ if acute pyelonephritis mother should be admitted and receive iv Abx

  ➔ 14days po Abx once afebrile then low-dose prophylactic Abx

  - Abx are safe during pregnancy?
    - penicillins are SAFE } eg ampicillin 500 qid, amoxicillin 250 tid
    - cephalosporins are SAFE } eg keflex 500 qid
    - nitrofurantoin SAFE EXCEPT IN T3 and if no hx of G6PD def. } eg 100mg qid
    - sulfonamides SAFE ONLY in T2 and if no hx of G6PD

- antibiotics should be avoided during pregnancy?
  - fluoroquinolones (cartilage damage in beagle pups)
  - tetracyclines (discoloured teeth, bone abN'ities)
  - chloramphenicol (grey baby syndrome □ hypoTN, hypothermia, CV collapse)
  - sulfonamides } not safe in T1 (NTDs) or T3 (kernicterus, hemolytic anemia)
  - aminoglycosides (deafness)
  - trimethoprim } not safe in T1 (structural defects – folic acid) or maybe T3 (megaloblastic anemia)
  - nitrofurantoin } not safe in T3 (hemolytic anemia)
  - ??? erythromycin (maternal cholestatic jaundice)
  - ??? flagyl (teratogenic) / recent data suggest they are safe

Table 3.5: Treatment regimens for asymptomatic bacteriuria and cystitis in pregnancy



Antibiotics	Duration of therapy	Comments
Nitrofurantoin (Macrobid®) 100 mg	q12 h, 3-5 days	Avoid in G6PD deficiency
Amoxicillin 500 mg	q8 h, 3-5 days	Increasing resistance
Co-amoxicillin/clavulanate	500 mg q12 h, 3-5 days	
Cephalexin (Keflex®) 500 mg	q8 h, 3-5 days	Increasing resistance
Fosfomycin 3 g	Single dose	
Trimethoprim	q12 h, 3-5 days	Avoid trimethoprim in first trimester/term

G6PD = glucose-6-phosphate dehydrogenase

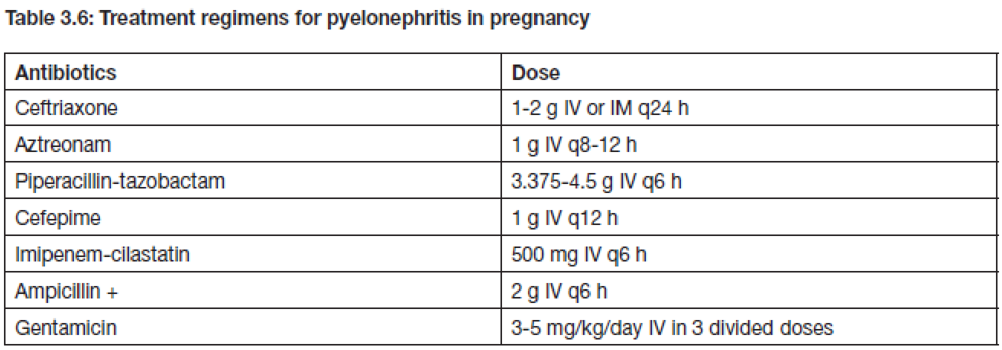


Table 3.6: Treatment regimens for pyelonephritis in pregnancy

Antibiotics	Dose
Ceftriaxone	1-2 g IV or IM q24 h
Aztreonam	1 g IV q8-12 h
Piperacillin-tazobactam	3.375-4.5 g IV q6 h
Cefepime	1 g IV q12 h
Imipenem-cilastatin	500 mg IV q6 h
Ampicillin +	2 g IV q6 h
Gentamicin	3-5 mg/kg/day IV in 3 divided doses

BACTERIURIA IN THE ELDERLY

- 20% of women and 10% of men older than 65yrs have bacteriuria
- most are asymptomatic
- different from pathogens seen in younger patients
    - E coli still most common } 75%
    - increased incidence of Proteus, Klebsiella, Enterobacter, Serratia, and Pseudomonas
    - gram +ve bacteriuria more common in elderly M than F
    - **polymicrobial bacteriuria more common in elderly**
- pyuria is sensitive but not specific in elderly } 60% with pyuria don't have bacteriuria
- screening for asymptomatic bacteriuria NOT RECOMMENDED in elderly (only recommended in pregnancy and prior to urologic procedure)
- **treatment of asymptomatic bacteriuria NOT RECOMMENDED, even in NH patients**
- 7days of Abx recommended, 14 days if febrile or systemic infection
- **goal is to eliminate symptoms but not necessarily to sterilize urine**
- elderly more susceptible to toxic and adverse effects of Abx therapy

URINARY TRACT INFECTIONS IN CHILDREN

9.1 Introduction

Urinary tract infection (UTI) represents the most common bacterial infection in children < 2 years of age.

In neonates, the symptoms differ in many aspects from those in UTIs in infants and children:

- The prevalence is higher.
- There is a male predominance.
- Infections not caused by *Escherichia coli* are more frequent.
- There is a higher risk of urosepsis.

Incidence:

- 3 ms old, UTIs in 7% of girls, 2% of circumcised boys, and 20% of uncircumcised boys presented with fever.
- 1st year, UTIs in boys (4%) > girls (2%).
- Later (prepupertal), girls (3%) > boys (1%).

Organism:

- ***E. coli*** in ~75% of UTIs (more frequent in community-acquired than nosocomial).
- In Nosocomial UTIs, *Klebsiella pneumoniae, Enterobacter* spp., *Enterococcus* spp., *Pseudomonas* spp. and *Candida* spp. are more frequent.
- Neonatal UTI is frequently complicated by bacteraemia.

Classification

five classification according to the site, episode, severity, symptoms and complicating factors.

For acute treatment, site and severity are most important.

1 ***Classification according to site***

- Lower urinary tract (cystitis) is an inflammatory condition of the urinary bladder with general signs and symptoms including dysuria, frequency, urgency, malodorous urine, enuresis, haematuria, and suprapubic pain.
- Upper urinary tract (pyelonephritis) is a diffuse pyogenic infection of the renal pelvis and parenchyma.
    - The onset of pyelonephritis is generally abrupt.
    - Clinical signs and symptoms include fever (≥ 38 °C), chills, costovertebral angle or flank pain, and tenderness.
    - Older children may report cystitis symptoms along with fever/flank pain.
    - Infants and children may have non-specific signs such as poor appetite, failure to thrive, lethargy, irritability, vomiting or diarrhoea.

2 ***Classification according to severity***

- In simple UTI, only mild pyrexia; able to take fluids and oral medication; slightly or not dehydrated; good expected level of compliance.
- In severe UTI, fever > 39°C, persistent vomiting, and moderate or severe dehydration.

3 Classification according to episode

- *First infection*: the first UTI may be a sign of anatomical anomalies that may predispose to complications of UTI and potential renal damage. Anatomical evaluation is recommended.
- *Recurrent infection*: (divided into unresolved and persistent infection):
  - ✓ In unresolved infection, initial therapy is inadequate for elimination of bacterial growth in the urinary tract due to:
    - inadequate therapy,
    - inadequate antimicrobial urinary concentration (poor renal concentration/ gastrointestinal malabsorption),
    - infection involving multiple organisms with differing antimicrobial susceptibilities].

  - ✓ Persistent infection is caused by re-emergence of bacteria from a site within the urinary tract coming from a nidus for persistent infection that cannot be eradicated
    - e.g. infected stones, non-functioning or poorly functioning kidneys/renal segments, ureteral stumps after nephrectomy, necrotic papillae in papillary necrosis, urachal cyst, urethral diverticulum, periurethral gland, vesicointestinal, rectourethral or vesicovaginal fistulas.
    - The same pathogen is identified in recurrent infections, but episodes of sterile urine may occur during and shortly following antimicrobial treatment.

- ✓ Reinfection:
    - caused by a variety of new infecting organisms, in contrast to bacterial persistence in which the same infecting organism is always isolated.
    - The most common general pathogenic species is *E. coli*, which occurs in many different serotypes. Therefore, recurrent *E. coli* UTI does not equate to infection with the same organism.

4 ***Classification according to symptoms***

- Asymptomatic bacteriuria indicates:
    - attenuation of uropathogenic bacteria by the host, or
    - colonisation of the bladder by non-virulent bacteria that are incapable of activating a symptomatic response.
- Symptomatic bacteriuria, include:
    - irritative voiding symptoms,
    - suprapubic pain (cystitis),
    - fever and malaise (pyelonephritis).

  Cystitis may represent early recognition of an infection destined to become pyelonephritis, or bacterial growth controlled by a balance of virulence and host response.

5 ***Classification according to complicating factors (12)***

- In uncomplicated UTI, in a patient with a morphologically and functionally normal urinary tract.
    - Mostly isolated or recurrent bacterial cystitis
    - usually associated with a narrow spectrum of infecting pathogens that are easily eradicated by a short course of oral antimicrobial agents.
    - Managed on an outpatient basis.

- In complicated UTI,
    - All **neonates**, patients with clinical **pyelonephritis**, and all children with known mechanical or functional **obstructions** of the urinary tract are considered to have complicated UTI.
        - Mechanical obstruction is commonly due to: PUV, strictures or stones.
        - Functional obstruction often results from lower urinary tract dysfunction of either neurogenic or non-neurogenic origin and dilating vesicoureteral reflux.
    - Patients require *hospitalization*, *parenteral antibiotics* and adequate *drainage* of the infected obstructed urinary tract.

Diagnosis

Medical history

Whether a primary (first) or secondary (recurring) infection; possible malformations of the urinary tract (e.g. pre- or postnatal ultrasound screening); family history; and whether there is **constipation** or presence of lower urinary tract symptoms.

Clinical signs and symptoms

- Non-specific symptoms (failure to thrive, jaundice, hyperexcitability and without any fever) in neonates with pyelonephritis or urosepsis can present with
- Fever (5% of children who present to a paediatric clinic).
- Septic shock is unusual, even with very high fever.
- Frequent voiding, dysuria and suprapubic, abdominal or lumbar pain (in children > 2 years old).

Physical examination

- General examination of the throat, lymph nodes, abdomen (constipation, palpable and painful kidney, or palpable bladder), flank, the back (stigmata of spina bifida or sacral agenesis), genitalia (phimosis, labial adhesion, vulvitis, epididymo-orchitis), and temperature.

Urine sampling, analysis and culture

- Before any antimicrobial.

Urine sampling

✚ In neonates, infants and non-toilet-trained children:

(1) *Plastic bag attached to the cleaned genitalia*.

- Helpful when the culture result is negative.
- Also, if the dipstick is negative for both leukocyte esterase and nitrite, or microscopic analysis is negative for both pyuria and bacteriuria, UTI can be excluded without the need for confirmatory culture.
- High incidence of false-positive results (85-99%) with unclean genitalia.

(2) *Clean-catch urine collection*.

- Holds a sterile foil bowl underneath the infant’s genitalia. offer oral fluids and urine collection is awaited.
- Time consuming and needs proper instruction of the parents.
- A false-positive rate of 5% and false-negative rate of 10%.

(3) *Bladder catheterisation*.

- Traumatic and bears the risk of nosocomial infection.

(4) *Suprapubic bladder aspiration*.

- The most sensitive method to obtain an uncontaminated urine sample in this age group so preferred in ill patients.
- Using ultrasound to assess bladder filling simplifies SPA and improves the diagnostic yield of obtaining a urine specimen from 60% to ~97%.
- Complications are rare (0.2%), ranging from transient haematuria to bowel perforation.

- In older, toilet-trained children, void on command:
    - *clean catch, especially midstream urine* after retracting the foreskin and cleaning the glans penis in boys and spreading the labia and cleaning the periurethral area in girls.

Blood sampling is dependent on the clinical situation.

Urinalysis

three methods used:

(1) Dipsticks:

- rapid results
- Includes:
    i. Leukocyte esterase (as a surrogate marker for pyuria).
    ii. nitrite (which is converted from dietary nitrates by most Gram-negative enteric bacteria in the urine, needs 4 hours)
        - Nitrite is not a very sensitive marker for infants, who empty their bladder frequently. Helpful when the result is positive, because it is highly specific.

The most frequent markers

Test	Sensitivity (Range), %	Specificity (Range), %
Leukocyte esterase test	83	78
Nitrite test	53	98
Leukocyte esterase or nitrite test positive	93	72
Microscopy, WBCs	73	81
Microscopy, bacteria	81	83
Leucocyte esterase test, nitrite test or microscopy positive	99	70

(2) Microscopy.

- The standard method of assessing pyuria after centrifugation of the urine with a threshold of 5 WBCs/HPF (25 WBC/µL).
- In uncentrifuged urine, $\geq$10 WBC/µL sensitive for UTI.

(3) Flow imaging analysis technology:

- classify particles in uncentrifuged urine specimens.
- The numbers of WBCs, squamous epithelial cells and red cells correlate well with those found by manual methods

Urine culture

- Not necessary after negative results for dipstick, microscopic or automated urinalysis, especially if there is an alternative source of fever. If the dipstick result is positive, confirmation by urine culture is recommended.
- It is unclear what represents a significant UTI.
  - Voided urine: if $> 10^5$ cfu/mL of voided urine.
    (The recent American Academy of Pediatric Guidelines on UTI: presence of both pyuria and at least 50 000 cfu).

- Catheterisation: 1,000-50,000 cfu/mL considered positive,
- SPA: Any counts obtained after considered as significant.
- Mixed cultures are indicative of contamination.
- Pyuria without bacteriuria (sterile pyuria) due to
  - incomplete antibiotic treatment,
  - urolithiasis, or foreign bodies in the urinary tract,
  - Infections caused by Mycobacterium tuberculosis or Chlamydia trachomatis.

Criteria for UTI in children (adapted from the EAU Guideline on Urological Infections):

Urine specimen from midstream void	**Urine specimen from bladder catheterisation**	**Urine specimen from suprapubic bladder puncture**
> 10^4 cfu/mL with symptoms > 10^5 cfu/mL without symptoms	> 1,000-50,000 cfu/mL	Any number of cfu/mL (at least 10 identical colonies)

Therapy

Administration route

- The choice between *oral* and *parenteral therapy* based on:
  - Patient age;
  - clinical suspicion of urosepsis; illness severity;
  - Complicated pyelonephritis (e.g. urinary obstruction).
  - Refusal of fluids, food and/or oral medication; vomiting; diarrhoea;
  - Non-compliance.
- In newborns and infants < 2 months, parenteral antibiotic therapy is recommended (increased incidence of urosepsis and severe pyelonephritis). Electrolyte disorders with hyponatremia and hyperkalaemia can occur in these cases.
- Combination treatment with ampicillin **and** an aminoglycoside (e.g. tobramycin or gentamicin) **or** a 3rd -generation cephalosporin achieves excellent therapeutic results (high efficacy of aminoglycosides, and cephalosporines against common uropathogens; enterococcus gap is closed with Ampillicin).
- A daily single dose of aminoglycosides is safe and effective (compared to the division in two doses).
- In uncomplicated nephritis, both oral and parenteral treatment can be considered, because both are equally effective in children without urinary tract abnormalities.

Duration of therapy

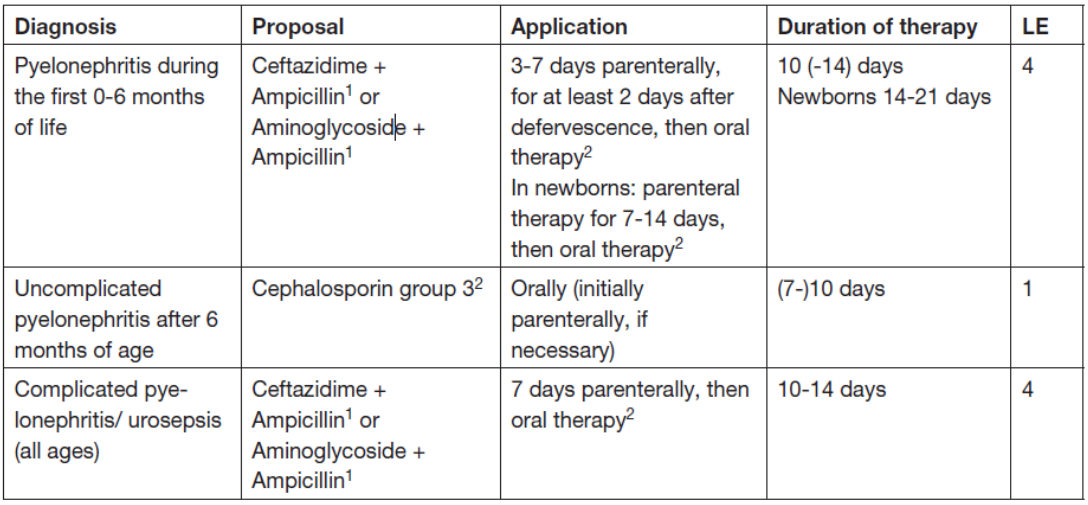
- Adequate treatment of UTI can prevent the spread of infection and renal scarring (by DMSA scan).
- Outcomes of short courses (1-3 days) inferior to 4-7-day course.
- A temporary urinary diversion (suprapubic cystostomy or percutaneous nephrostomy) are used in case of failure of conservative treatment in obstructive uropathy.
- ***Acute focal bacterial nephritis (lobar nephronia)***:
    - A localised bacterial infection of the kidney that presents as an inflammatory mass without abscess formation.
    - This may represent a relatively early stage of renal abscess.
    - For the majority of children, the pathogenesis is related to ascending infection due to preexisting uropathy, especially vesicorenal reflux or urinary obstruction (megaureter).
    - Prolonged intravenous or oral antibiotic treatment (acc. To culture) is sufficient in most cases.

Antimicrobial agents

Frequently used antibacterial substances for the therapy of urinary tract infections in infants and children*

Chemotherapeutics	Daily dosage	Application	Comments
Parenteral cephalosporins			
Group 3a, e.g. cefotaxime	100-200 mg/kg *(Adolesc.: 3-6 g)*	i.v. in 2-3 D	
Group 3b, e.g. ceftazidime	100-150 mg/kg *(Adolesc.: 2-6 g)*	i.v. in 2-3 D	
Ceftriaxone	75 mg/kg,	i.v. in 1 D	
Oral cephalosporins			
Group 3, e.g. ceftibuten	9 mg/kg *(Adolesc.: 0,4 g)*	p.o. in 1-2 D p.o. in 1-2 D	
Group 3, e.g. cefixime	8-12 mg/kg *(Adolesc.: 0,4 g)*	p.o. in 1-2 D	
Group 2, e.g. cefpodoxime proxetil	8-10 mg/kg *(Adolesc.: 0,4 g)*	p.o. in 2D	
Group 2, e.g. cefuroximaxetil	20-30 mg/kg (Adolesc.: 0,5-1 g)	p.o. in 3 D	
Group 1, e.g. cefaclor	50 -100 mg/kg *(Adolesc.: 1,5-4 g)*	p.o. in 2-3 D	
Trimethoprim or Trimethoprim/sulfamethoxazole	5-6 mg/kg 5-6 mg/kg (TMP-Anteil) *(Adolesc.: 320 mg)*	p.o. in 2 D p.o. in 2 D	
Ampicillin	100-200 mg/kgKG *(Adolesc.: 3-6 g)*	i.v. in 3 D i.v. in 3-4 D	Ampicillin and Amoxicillin are not eligible for calculated therapy
Amoxicillin	50-100 mg/kg *(Adolesc.: 1,5-6 g)*	p.o. in 2-3 D[1] p.o. in 2-3 D	
Amoxicillin/clavulanic acid (parenteral)	60-100 mg/kg *(Adolesc.: 3,6-6,6 g)*	i.v. in 3 D i.v. in 3 D	
Amoxicillin/clavulanic acid (oral)	45-60 mg/kg (Amoxicillin-fraction) *(Adolesc.: 1500 + 375 mg)*	p.o. in 3 D p.o.in 3 D	
Piperacillin	300 mg/kg	i.v. in 3-4 D	
Tobramycin	5 mg/kg *(Adolesc.: 3-5 mg/kg, max. 0,4 g)*	i.v. in 1 D	Drug monitoring
Gentamicin	5 mg/kg *(Adolesc.: 3-5 mg/kg, max. 0,4g)*	i.v. in 1 D	
Ciprofloxacin	Children and adolesc. (1-17 years of age): 20-30 mg/kg (max. D: 400 mg) (parenterally) Children and adolesc. (1-17 years of age): 20-40 mg/kg (max. D 750 mg) (orally)	i.v. in 3 D p.o. in 2 D	Approved in most European countries as second- or third line medication for complicated UTIs, „reserve-antibiotic“ !
Nitrofurantoin	3-5 mg	p.o. in 2 D	Contraindicated in the case of renal insufficiency

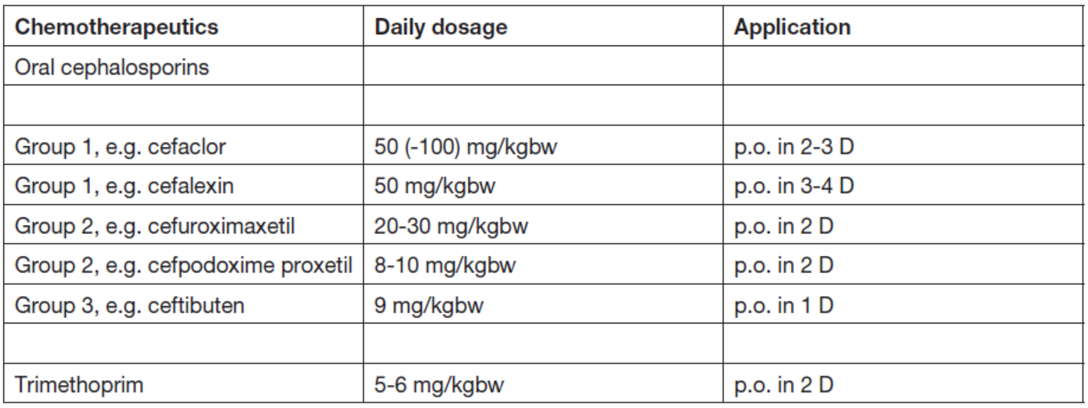
Recommendations for calculated antibacterial therapy of pyelonephritis dependent on age and severity of the infection

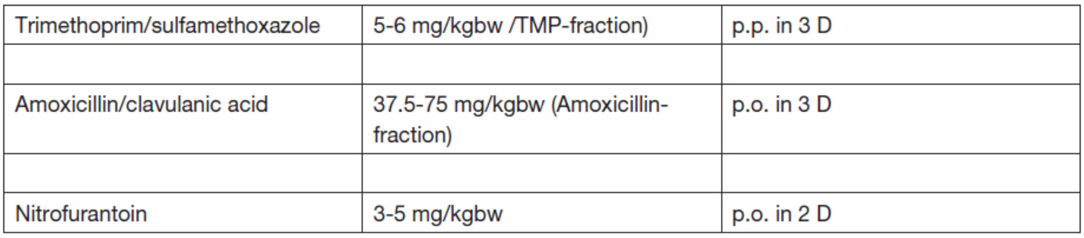


Diagnosis	Proposal	Application	Duration of therapy	LE
Pyelonephritis during the first 0-6 months of life	Ceftazidime + Ampicillin[1] or Aminoglycoside + Ampicillin[1]	3-7 days parenterally, for at least 2 days after defervescence, then oral therapy[2] In newborns: parenteral therapy for 7-14 days, then oral therapy[2]	10 (-14) days Newborns 14-21 days	4
Uncomplicated pyelonephritis after 6 months of age	Cephalosporin group 3[2]	Orally (initially parenterally, if necessary)	(7-)10 days	1
Complicated pyelonephritis/ urosepsis (all ages)	Ceftazidime + Ampicillin[1] or Aminoglycoside + Ampicillin[1]	7 days parenterally, then oral therapy[2]	10-14 days	4

Recommendations for antibacterial treatment in cystitis und cystourethritis

(Dosages for children up to 12 years of age)



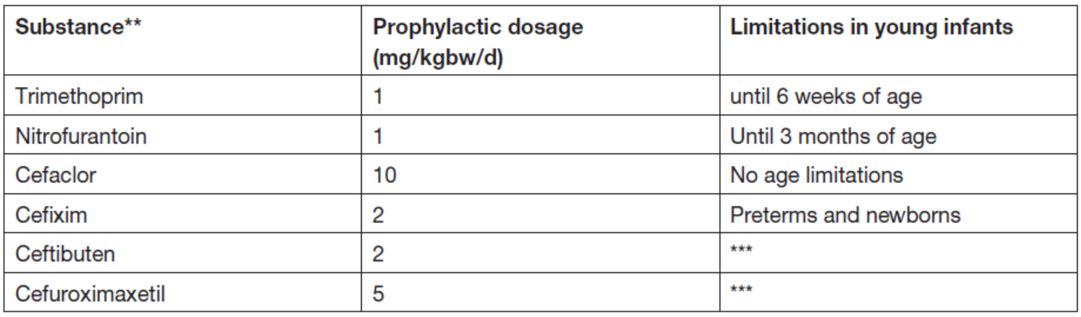


Chemotherapeutics	Daily dosage	Application
Oral cephalosporins		
Group 1, e.g. cefaclor	50 (-100) mg/kgbw	p.o. in 2-3 D
Group 1, e.g. cefalexin	50 mg/kgbw	p.o. in 3-4 D
Group 2, e.g. cefuroximaxetil	20-30 mg/kgbw	p.o. in 2 D
Group 2, e.g. cefpodoxime proxetil	8-10 mg/kgbw	p.o. in 2 D
Group 3, e.g. ceftibuten	9 mg/kgbw	p.o. in 1 D
Trimethoprim	5-6 mg/kgbw	p.o. in 2 D
Trimethoprim/sulfamethoxazole	5-6 mg/kgbw /TMP-fraction)	p.p. in 3 D
Amoxicillin/clavulanic acid	37.5-75 mg/kgbw (Amoxicillin-fraction)	p.o. in 3 D
Nitrofurantoin	3-5 mg/kgbw	p.o. in 2 D

Chemoprophylaxis

- Long-term antibacterial prophylaxis considered in cases of high susceptibility to UTI and risk of acquired renal damage E.g. trimethoprim-sulfamethoxazole (even from birth).

Drugs for antibacterial prophylaxis



Substance**	**Prophylactic dosage (mg/kgbw/d)**	**Limitations in young infants**
Trimethoprim	1	until 6 weeks of age
Nitrofurantoin	1	Until 3 months of age
Cefaclor	10	No age limitations
Cefixim	2	Preterms and newborns
Ceftibuten	2	***
Cefuroximaxetil	5	***

Monitoring of UTI

- With successful treatment → Sterile urine after 24 h and leukocyturia disappears within 3-4 days.
- Fever disappears within 24-48 h. If prolonged fever → treatment-resistant uropathogens or the presence of congenital uropathy or acute urinary obstruction. Immediate ultrasound is recommended.
- ***Procalcitonin*** (among other laboratory inflammatory parameters such as C-reactive protein and leukocyte count) can be used as reliable serum marker for early prediction of renal parenchymal inflammation with first febrile UTI.
- In patients with febrile UTI, serum electrolytes and blood cell counts should be obtained.

Imaging

Ultrasound

- Renal and bladder ultrasonography is strongly recommended in infants with febrile UTI to exclude obstruction of the upper and lower urinary tract.
- Post-void residual urine should be measured in toilet-trained children to exclude voiding abnormalities as a cause of UTI.

Radionuclide scanning

- Changes in DMSA clearance during acute UTI indicate *pyelonephritis or parenchymal damage*, correlated well with the presence of dilating reflux and the risk of further pyelonephritis episodes, break-through-infections and future renal scarring.
- In neonates, after the first symptomatic, community-acquired UTI, the majority of renal units with VUR grade III or higher had normal early DMSA scanning.

Voiding cystourethrography

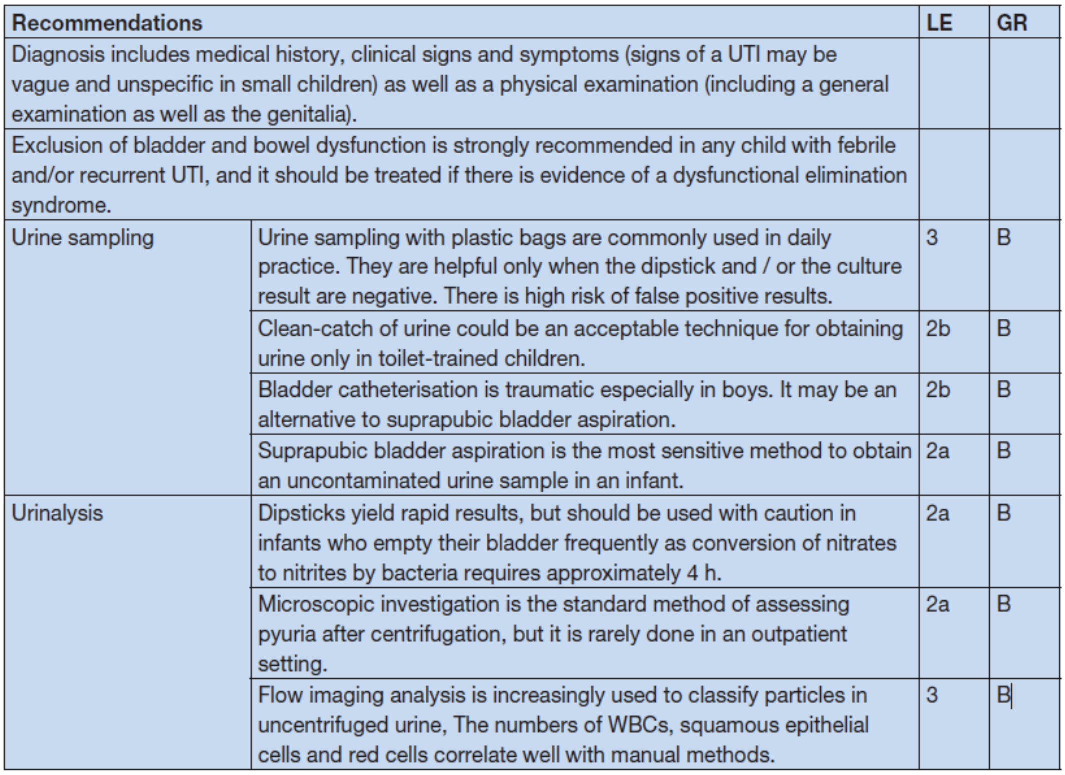
- Voiding cystourethrography is still the gold standard to exclude or confirm VUR (Dilating VUR is missed by ultrasound in around one third of cases).
- Due to renal scarring risk, VCUG is recommended **after the first episode of febrile UTI in boys and girls** (no morbidity proven).
- The timing of VCUG does not influence the presence or severity of VUR.
- Another option is doing DMSA first, followed by VCUG if there is renal cortical uptake deficiency after urinary tract infection.

Bladder and bowel dysfunction

- Are risk factors for which each child with UTI should be screened upon presentation.
- Normalisation of micturition disorders or bladder overactivity is important to lower the rate of UTI recurrence.
- If there are signs of bladder and/or bowel dysfunction at infection-free intervals, further diagnosis and effective treatment are strongly recommended (65-68).
- Treatment of constipation leads to a decrease in UTI recurrence.
- Therefore, exclusion of bladder and bowel dysfunction is strongly recommended in any child with febrile and/or recurrent UTI, and it should be treated if there is evidence of a dysfunctional elimination syndrome.

Conclusions and recommendations for UTI in children

Conclusions
Urinary tract infection represents the most common bacterial infection in children < 2 years of age. The incidence varies depending on age and sex.
Classifications can be made according to the site, episode, severity, symptoms and complicating factors. For acute treatment, site and severity are most important.
The number of colony forming units (cfu) in the urine culture can vary and be related to the method of specimen collection, diuresis, and time and temperature of storage until cultivation occurs. The classical definition of > 105 cfu/mL of voided urine is still used to define a significant UTI.



Recommendations		LE	GR
Diagnosis includes medical history, clinical signs and symptoms (signs of a UTI may be vague and unspecific in small children) as well as a physical examination (including a general examination as well as the genitalia).			
Exclusion of bladder and bowel dysfunction is strongly recommended in any child with febrile and/or recurrent UTI, and it should be treated if there is evidence of a dysfunctional elimination syndrome.			
Urine sampling	Urine sampling with plastic bags are commonly used in daily practice. They are helpful only when the dipstick and / or the culture result are negative. There is high risk of false positive results.	3	B
	Clean-catch of urine could be an acceptable technique for obtaining urine only in toilet-trained children.	2b	B
	Bladder catheterisation is traumatic especially in boys. It may be an alternative to suprapubic bladder aspiration.	2b	B
	Suprapubic bladder aspiration is the most sensitive method to obtain an uncontaminated urine sample in an infant.	2a	B
Urinalysis	Dipsticks yield rapid results, but should be used with caution in infants who empty their bladder frequently as conversion of nitrates to nitrites by bacteria requires approximately 4 h.	2a	B
	Microscopic investigation is the standard method of assessing pyuria after centrifugation, but it is rarely done in an outpatient setting.	2a	B
	Flow imaging analysis is increasingly used to classify particles in uncentrifuged urine, The numbers of WBCs, squamous epithelial cells and red cells correlate well with manual methods.	3	B

Treatment	The choice between oral and parenteral therapy should be based on patient age; clinical suspicion of urosepsis; illness severity; refusal of fluids, food and/or oral medication; vomiting; diarrhoea; non-compliance; and complicated pyelonephritis (e.g., urinary obstruction).		
	Long-term antibacterial prophylaxis should be considered in cases of high susceptibility to UTI and risk of acquired renal damage.		
	Parenteral therapy is advised when there is clinical suspicion of urosepsis; illness severity; refusal of fluids, food and/or oral medication; vomiting; diarrhoea; non-compliance; and complicated UTI. As a result of the increased incidence of urosepsis and severe pyelonephritis in newborns and infants aged < 2 months, parenteral antibiotic therapy is recommended. In an emergency setting, i.v. fluid replacement is necessary.	2a	B
	Outcomes of short courses (1-3 days) are inferior to those of 7-4-day courses. Oral therapy with a third-generation cephalosporin (e.g., cefixime or ceftibuten) may be equivalent to the usual 2-4 days intravenous therapy followed by oral treatment. In complicated UTI, parenteral treatment with broad-spectrum antibiotics is indicated.	1b	B
Imaging	Renal and bladder ultrasonography is strongly recommended in infants with febrile UTI to exclude obstruction of the upper and lower urinary tract.	3	B
	Changes in DMSA clearance during acute UTI indicate pyelonephritis or parenchymal damage. If it is positive, reflux may be present.	2b	B
	VCUG is the gold standard to exclude or confirm VUR. Due to the risk of renal scarring, it is recommended after the first episode of febrile UTI in boys and girls. The timing of VCUG does not influence the presence or severity of VUR.	2a	B

CATHETER-ASSOCIATED BACTERIURIA

- most common nosocomial infection } accounts for ~40%
- inevitable & occurs at ~10% per day of catheterization } febrile episodes occur only 1 per 100days
- usually asymptomatic
- route of infection
    - introduced with initial catheterization } urethral bacteria or poor technique
    - retrograde colonization from Foley bag } intraluminal route to bladder
- causative pathogens

  ➔ bacteria w/in urine can differ from bacterial biofilm on catheter
    - Pseudomonas & Proteus common biofilm pathogens
    - E coli still most common
    - Pseudomonas, Proteus, and enterococcus more common
    - polymocrobial bacteriuria very common
- management of catheter-associated bacteriuria
    - no Abx recommended if catheter to stay indwelling for >3-4days
    - Abx treatment only if symptomatic UTI
    - send urine C&S before initiating Abx therapy
    - stop within 48hrs of resolution of infection
    - catheter should be changed
    - Abx around time of catheter change or removal recommended for 2-3 days

MANAGEMENT OF UTIs IN PATIENTS WITH SPINAL CORD INJURY

- roughly 33% have bacteriuria at any one time
- UTI is the most common cause of fever in SCI patient
- Why is CIC preferred over indwelling catheterization in SCI patients?
    - lower incidence of bacteriuria
    - less complications with fever, bacteremia, and local infections (eg prostatitis)
    - reduces incidence of stones
    - maintains low bladder pressures

  ➔ S/P catheters next best, followed by condom catheters
- most are asymptomatic
    - don’t have irritative symptoms because of a loss of sensation
    - often complain of flank or back pain or abdo discomfort
    - leakage between catheterizations increased spasticity
    - cloudy, smelly urine
- u/a usually shows bacteriuria and pyruia } pyuria alone may be from catheterizations
- causative pathogens
    - E coli found in ~20%
    - Enterococci, Proteus mirabilis, and Pseudomonas much more common
    - Klebsiella, Serratia, Candida are also common
    - Providencia stuartii rarely found outside long- catheterized GU tract
    - often have polymicrobial infections

- ttt
    - **ONLY SYMPTOMATIC PATIENTS NEED ABX**
    - urine culture MUST be obtained BEFORE administration of ABx
    - high rate of resistance and often diverse flora
- for afebrile patients,
    - oral fluoroquinolone is Abx of choice
    - indwelling catheters should be changed
- if febrile,
    - patients should be admitted and started on iv Abx (eg amp + gentamicin/ceftriaxone).
    - if no clinical improvement by 24-48hrs, then reculture and adjust Abx based on initial urine C&S
    - consider imaging to r/o obstruction, stones, abscess
    - 4-5days Abx for most, 10-14days if febrile
- post-Abx cultures NOT RECOMMENDED because of high rate of re-colonization except with urease-producing bacteria
- SCI patients w/ recurrent UTIs need imaging & UDS testing with review of sterile techniques
- **NO ABX PROPHYLAXIS RECOMMENDED**

- What is the risk of bladder cancer with chronically catheterized patients?
    - risk of developing SCC of bladder with chronic catheter or chronic infections
    - risk evident usually after 5-10yrs
    - chronic inflammation of mucosa may be carcinogenic stimulus
    - nitrosamines produced in infected urine may also play a part

OTHER INFECTIONS

Fournier's Gangrene

Def:

- necrotizing fasciitis of the genitalia & perineum
- often abrupt onset of a rapidly fulminating genital gangrene } can be indolent onset
- source of infection is most commonly from skin, urethra, or rectal regions
- bacteria pass through Buck's fascia and spread along dartos fascia of scrotum & penis, Colles' fascia of perineum, and Scarpa's fascia of anterior abd. wall

RFs

- Old age, Obesity, Malnutrition, Alcohol abuse
- DM, Immunosuppression (eg HIV)
- Paraphimosis, CIC (urine extravasation), Trauma
- Surgery in local area, Perianal disease
- PVD

Causative organism:

- most commonly mixed bacterial growth
- E coli most common single pathogen

C/P

- hx
  - of recent perineal trauma, instrumentation, urethral stricture associated with STD or urethrocutaneous fistula
  - hx of perirectal disease } fissures, pain, rectal bleeding, etc

- starts with local cellulitis that spreads deeper
- presents with pain, fever, and systemic toxicity (mental status changes, tachypnea, tachycardia

Inv.

- lab
  - anemia
  - elevated creatinine
  - hypoNa, hypoCa
  - culture urine, blood, and site of infection
- Rad.:
  - plain film Xray may show subcutaneous air
  - U/S or CT may also be good to demonstrate air

ttt:

Prompt Dx is critical

- Medical:
  - ABCs
  - iv fluids
  - broad spectrum Abx } ampicillin + ceftriaxone + flagyl
- Surgical
  - **immediate surgical debridement**
    - all necrotic skin, fascia, fat must be excised & wound left open
    - repeat debridement in 24-48hrs PRN
    - orchiectomy almost never required b/c testes have own blood supply
    - place testicles in thigh pouch or wrap in moist NS-soaked gauze

- S/P tube if urethral trauma or extravasation suspected
- colostomy if colonic or rectal communication
- hyperbaric O2 has been shown to improve outcomes

➔ once wound has healed, may need reconstruction to close defect if large eg myocutaneous flap

Prognosis:

- mortality rate is ~20% } higher if DM, EtOH'ic, and those w/ colorectal source of infection

Periurethral abscesses

- life-threatening condition of M urethra and periurethral tissues
- frequently a result of gonorrhea, urethral strictures, or urethral CIC
- urine source of infection gram–ve, enterococci, and anaerobes
- C/P
    - initially localized by Buck's fascia to a small area
    - once it penetrates through Buck's, it can spread rapidly from buttocks posteriorly to clavicles superiorly
    - usually have scrotal swelling and fever
    - sometimes have AUR, spontaneously draining abscess, or urethral symptoms
- Inv.
    - urinalysis shows bacteriuria and pyuria
- ttt
    - immediate S/P drainage
    - iv hydration
    - iv ABx } ampicillin + gentamicin/ceftriaxone
    - wide debridement

URETHRITIS

Epidemiology

- gonorrhoeal urethritis different from non-specific urethritis.
- spread by sexual contact.

Pathogens

- ***N. gonorrhoeae, C. trachomatis, Mycoplasma genitalium* and *Trichomonas vaginalis***.
- *Mycoplasma hominis* rarely cause urethritis, and *Ureaplasma urealyticum* (infrequent cause).

Route of infection and pathogenesis

- Causative agents either
  - remain extracellularly on the epithelial layer or
  - penetrate into the epithelium (*N. gonorrhoeae* and *C. trachomatis*) and cause pyogenic infection.
- chlamydiae and gonococci can spread further to cause epididymitis in men or cervicitis, endometritis and salpingitis in women.
- *Myc. genitalium* can also cause cervicitis and pelvic inflammatory disease in women.

C/P

- **Mucopurulent or purulent discharge**, **alguria**(painful urinating), **dysuria** and **urethral pruritus**
- **asymptomatic** (common).

Inv.

- Lab
  - A **Gram stain of a urethral discharge or a urethral smear** >5 WBCs/HPF (× 1,000), and gonococci located intracellularly as G-ve diplococci, indicate **pyogenic urethritis**.
  - A **positive leukocyte esterase test or > 10 leucocytes per high power field** (× 400) in the first voiding urine specimen diagnostic.
  - **First voiding urine specimen** used instead of a urethral smear
  - *Trichomonas* sp. can usually be identified microscopically.

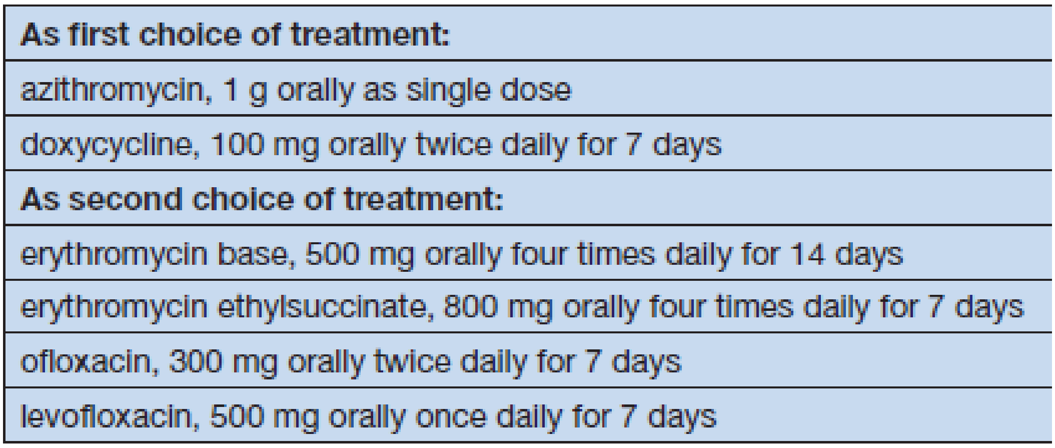
Therapy

Treatment of gonorrhoeal urethritis

- **As first-choice treatment**
  - **ceftriaxone, 1 g intramuscularly** (with local anaesthetic) as a single dose;
  - **azithromycin, 1 g orally** as a single dose
- **Alternative regimens**
  - ciprofloxacln, 500 mg orally as single dose;
  - ofloxacin, 400 mg orally as single dose;
  - levofloxacin, 250 mg orally as single dose.

- Note that fluoroquinolones are contraindicated in adolescents (< 18 years) and pregnant women.
- spread of fluoroquinolone-resistant *N. gonorrhoeae*
- Because gonorrhoeae is frequently accompanied by chlamydial infection, **an active antichlamydial therapy should be added**.

Treatment of non-gonorrhoeal urethritis



As first choice of treatment:
azithromycin, 1 g orally as single dose
doxycycline, 100 mg orally twice daily for 7 days
As second choice of treatment:
erythromycin base, 500 mg orally four times daily for 14 days
erythromycin ethylsuccinate, 800 mg orally four times daily for 7 days
ofloxacin, 300 mg orally twice daily for 7 days
levofloxacin, 500 mg orally once daily for 7 days

- **Doxycycline and/or azithromycin** for **chlamydial infections**
- ***Myc. genitalium*** → azithromycin.
- **In pregnant women**, (NO fluoroquinolones or doxycycline).
  - erythromycin, azithromycin and amoxicillin 500 mg three times daily for 7 days can be used.
- If therapy fails, consider ***T. vaginalis* and/or *Mycoplasma***
  - combination of metronidazole (2 g orally as single dose) and erythromycin (500 mg orally four times daily for 7 days).
  - As in other STDs, treatment of sexual partners is necessary.

Follow-up and prevention

- Patients should return for evaluation if symptoms persist or recur after completion of therapy.
- Stop sexual intercourse until 7 days after therapy is initiated.
- Persons who have been diagnosed with a new STD should receive testing for other STDs, including syphilis and HIV.

Bacterial Prostatitis

Introduction and definition

- **Prostatitis** included both acute and chronic bacterial prostatitis, in which an infective origin is accepted
- The term **prostatitis syndrome (recently, CPPS)** → no infective agent can be found (multifactorial origin, mostly obscure).
- Prostatitis and CPPS are diagnosed by symptoms and evidence of inflammation and infection localised to the prostate.
- A causative pathogen detected by routine methods in **only 5-10%** and treated by antimicrobial therapy (others ttt empirically).

Incidence:

- **most common urologic Dx in men <50yrs (mostly prostatitis)**
- 3rd most common urologic Dx in men >50yrs of age (BPH, PCa).
- more common in the 20-50 age range and if >70yrs old

Pathology:

- Histopathology of prostatitis:
  - **stromal lymphocytic infiltrate immediately adjacent to prostatic acini (most common pattern)**
  - ↑'d number of inflammatory cells, may be prostatic stones.

Etiology of prostatitis: مهمه

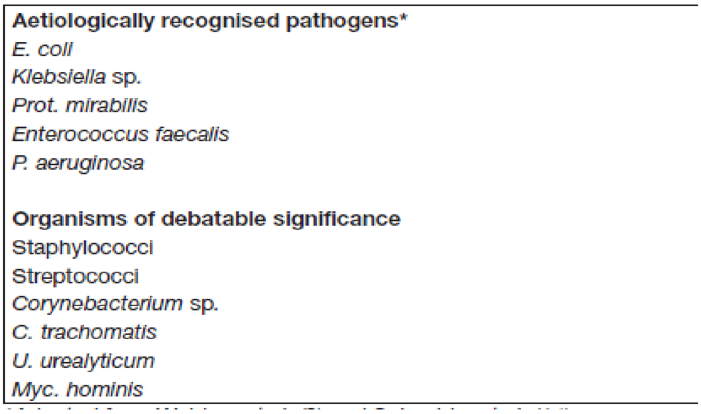
1) Microbiologic causes
   - **bacteria cultured in only ~10% of cases**
   - gram -ve } Enterobacteriaceae (most common in acute bact. Prostatitis *(E. coli* (most common), *Pseudomonas, Serratia, Klebsiella, Enterobacter)*
   - gram +ve } mainly Enterococcus
   - *corynebacterium* (hard to culture, gram-variable pleomorphic coccobacillary rods)

N.B:

In chronic bacterial prostatitis, the spectrum of strains is wider. The significance of intracellular bacteria as *C. trachomatis*, is uncertain.

immune def. Pts, prostatitis d.t fastidious pathogens, such as *M. tuberculosis*, *Candida* sp. and rare pathogens, such as *Coccidioides immitis*, *Blastomyces dermatitidis*, and *Histoplasma capsulatum*

Table 10.4: Most common pathogens in prostatitis



Aetiologically recognised pathogens*
E. coli
Klebsiella sp.
Prot. mirabilis
Enterococcus faecalis
P. aeruginosa
Organisms of debatable significance
Staphylococci
Streptococci
Corynebacterium sp.
C. trachomatis
U. urealyticum
Myc. hominis

2) **I**ntraprostatic ductal reflux
3) **C**hemically-induced inflammation (refluxing urine causes infl.)
4) **I**mmunologic alterations
5) **P**sychological cause
6) **D**ysfunctional voiding (anatomic or neurophysiologic obstruction)
7) **I**nterstitial cystitis-like cause
8) **A**ltered prostatic host defense ("CAT PUBES")
    - **C**atheters, **T**RUS/TURP, **U**TIs, **E**pididymitis (acute)
    - **A**nal sex (unprotected)
    - **P**himosis
    - **B**lood groups (certain types more susceptible)
    - **S**ecretory dysfunction of prostate
    - low fructose, citric acid, Zn, Mg, Ca **or**
    - increased pH, C3, LDH-5
9) **N**eural dysregulation/pelvic floor musculature abN'ities:
    - dissociation between CNS and pelvic floor muscles
    - pain at pelvic musculature attachment sites (sacrum, coccyx, ischial tuberosity, pubic rami, etc)
    - pudendal nerve entrapment, myofascial trigger points
10) **M**ultifactorial cause

Classification:

Traditional classification of prostatitis based on Meares-Stamey 4-glass test

TYPE	Name	Purulent prostatic fluid (VB3)	Cultured bacteria	Systemic signs
type 1	Acute bacterial prostatitis	+	+	+
type 2	Chronic bacterial prostatitis	+	+	-
type 3	Non-bacterial prostatitis	microscopic WBC	-	-
type 4	Prostadynia (symptoms only)	-	-	-

New Classification of prostatitis and CPPS according to NIDDK/NIH

- **category I = acute bacterial prostatitis**
- **category II = chronic bacterial prostatitis**
- **category III = "chronic pelvic pain syndrome (CPPS)"** No Bact.

(def. chronic GU PAIN in absence of uropathogenic bacteria localized to prostate)

- **IIIA**: **inflammatory CPPS**
  - pain + WBCs (>5-10/HPF in VB3 or semen)
- **IIIB**: **non-inflammatory prostatitis (prostadynia)**
  - pain but NO WBCs (>5-10/HPF in VB3 or semen)

- category IV = asymptomatic inflammatory prostatitis

- NO PAIN + WBCs +/- bacteria in VB3 urine or semen or tissue Bx's

C/P

- *Symptom questionnaires*
  - The **Chronic Prostatitis Symptom Index (CPSI)**, by the **International Prostatitis Collaborative Network (IPCN)**.
    - **9 questions looking at 3 domains**
      a. **pain (4)** } location, frequency, severity
      b. **urinary function (2)** } irritative, obstructive
      c. **QOL/impact (3)**
      d. 6 points or 25% decrease = significant improvement

- ***Symptoms***

1) Category I:

- acute onset of pain (perineal, S/P, genital) + LUTS + systemic febrile illness +/- septicemia (5% → chronic bacterial prostatitis)

2) Category II:

- recurrent UTI or CPPS history is common
- Asymptomatic bet. acute episodes

3) Category IIIA and IIIB (can’t distinguish IIIA from IIIB)

- **Pain** (perineal, S/P, genital, low back, **during or after ejaculation**)
- LUTS, ED
- **“chronic” if symptoms last >3months**

4) Category IV (no symptoms**)**

- present with BPH, elevated PSA, PCa, infertility.

- Examination

- **In acute prostatitis**, the prostate: swollen and tender on DRE. (Prostatic massage is contraindicated) → exclude prostatic abscess.
- **Otherwise,** the prostate is usually normal on palpation.

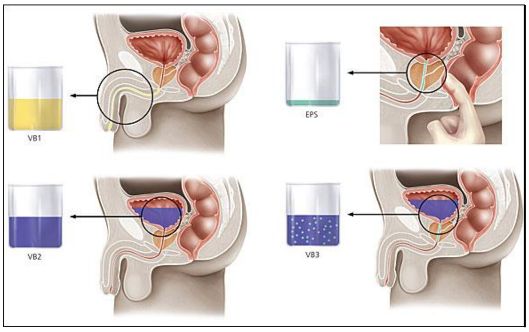
Work-up for prostatitis

- Mandatory

- History & Physical , Urinalysis, Urine C&S

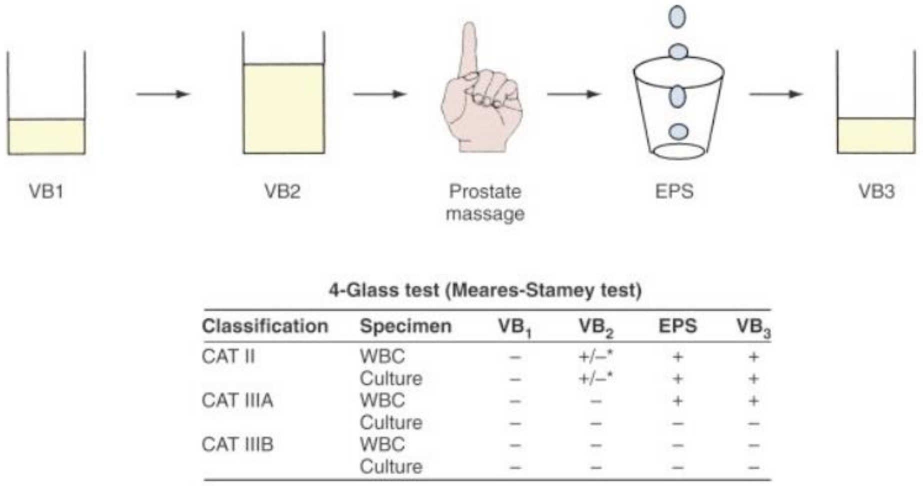
- Recommended

- **Stamey test**
- Questionnaire (CPSI)
- Uroflow & PVR
- Urine cytology



Other tests (mainly in research only):

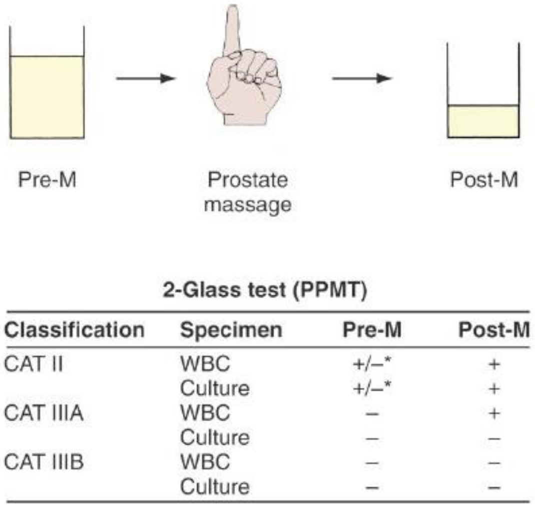
- **serum immunologic testing (antibodies, IL-1, etc)**
- **Zn levels**
- **+ve rRNA-based signals**



4-Glass test (Meares-Stamey test)

Classification	Specimen	VB_1	VB_2	EPS	VB_3
CAT II	WBC	–	+/–*	+	+
	Culture	–	+/–*	+	+
CAT IIIA	WBC	–	–	+	+
	Culture	–	–	–	–
CAT IIIB	WBC	–	–	–	–
	Culture	–	–	–	–

→ MEARES-STAMEY 4-GLASS TEST



2-Glass test (PPMT)

Classification	Specimen	Pre-M	Post-M
CAT II	WBC	+/–*	+
	Culture	+/–*	+
CAT IIIA	WBC	–	+
	Culture	–	–
CAT IIIB	WBC	–	–
	Culture	–	–

→ 2-GLASS TEST

Diagnosis:

- ***History and symptoms***
  - Acc. to the duration of symptoms, bacterial prostatitis is described as either acute or chronic (> 3 months).
  - Predominant symptoms are pain and LUTS.
- Lab.:
  - ***Urine cultures and expressed prostatic secretion*** (EPS):
    - In acute prostatitis: **mid-stream urine culture** most important.

  - In chronic bacterial prostatitis→ localisation cultures and microscopy of the segmented urine and of **expressed prostatic secretion (EPS)** by Meares and Stamey.
  - In case of suspected prostate tuberculosis → urine PCR.

- *Rad.*
  - Transrectal ultrasound (TRUS) → intraprostatic abscesses, prostate calcifications, and dilated SVs (unreliable diag. tool in prostatitis).

- ***Prostate biopsy***
  - Perineal biopsies **cannot be recommended** (research purposes).
  - Transrectal prostate biopsy (not advised in bacterial prostatitis).

- ***Additional investigations***
  - **Ejaculate analysis**
  - not recommended for microbiological investigation due to the low sensitivity and specificity compared to the 2- or 3-glass tests.
  - for a generalised male accessory gland infection (MAGI)

  - **Uroflowmetry, retrograde urethrography, or endoscopy →** Rule out bladder outflow and urethral obstruction
  - ***Prostate Specific Antigen (PSA)***
    - increased in acute bacterial prostatitis and other urogenital inf.
    - elevated PSA d.t prostatic inflammation normalise after antimicrobial treatment for 4 weeks in about 50% of patients

    - A delay of at least 3 months should be allowed before it can be assumed that a stable level of PSA has been reached.

    - Measurement of free and total PSA adds no practical diagnostic information in prostatitis.

Treatment

Medical Rx

1) Abx (best duration??!! 2-3 w minimum)

- **life-saving** in acute bact. prostatitis, **recommended** in ch. Bact. prostatitis.
- initial acute infection
  - amp + gent **or** 2nd, 3rd G. cephalosporin **or** fluoroquinolone
- chronic bacterial prostatitis
  - trimethoprim or fluoroquinolone
- NOT RECOMMENDED for previously treated men with non-bacterial CP/CPPS of long duration.
- **Intraprostatic injection of antibiotics (under trial)**

2) α-blockers (eg flomax)

→ moderate benefit on RCTs

- improve outflow obstruction
- diminish intraprostatic ductal reflux
- combination therapy with Abx or anti-inflammatories → better

3) Phytotherapies

→ little benefit on RCTs

4) **Hormonal therapies** (eg finasteride, estrogens)

- not recommended as monotherapy.

5) Anti-inflammatories

→little benefit on RCTs

- decreases infl. w/in prostate (NSAIDs, steroids, immunosuppression).

- rofecoxib, celecoxib, pentosan polysulfate, prednisone, etc

6) Pentosan polysulfate

7) **M**uscle relaxants (eg baclofen)

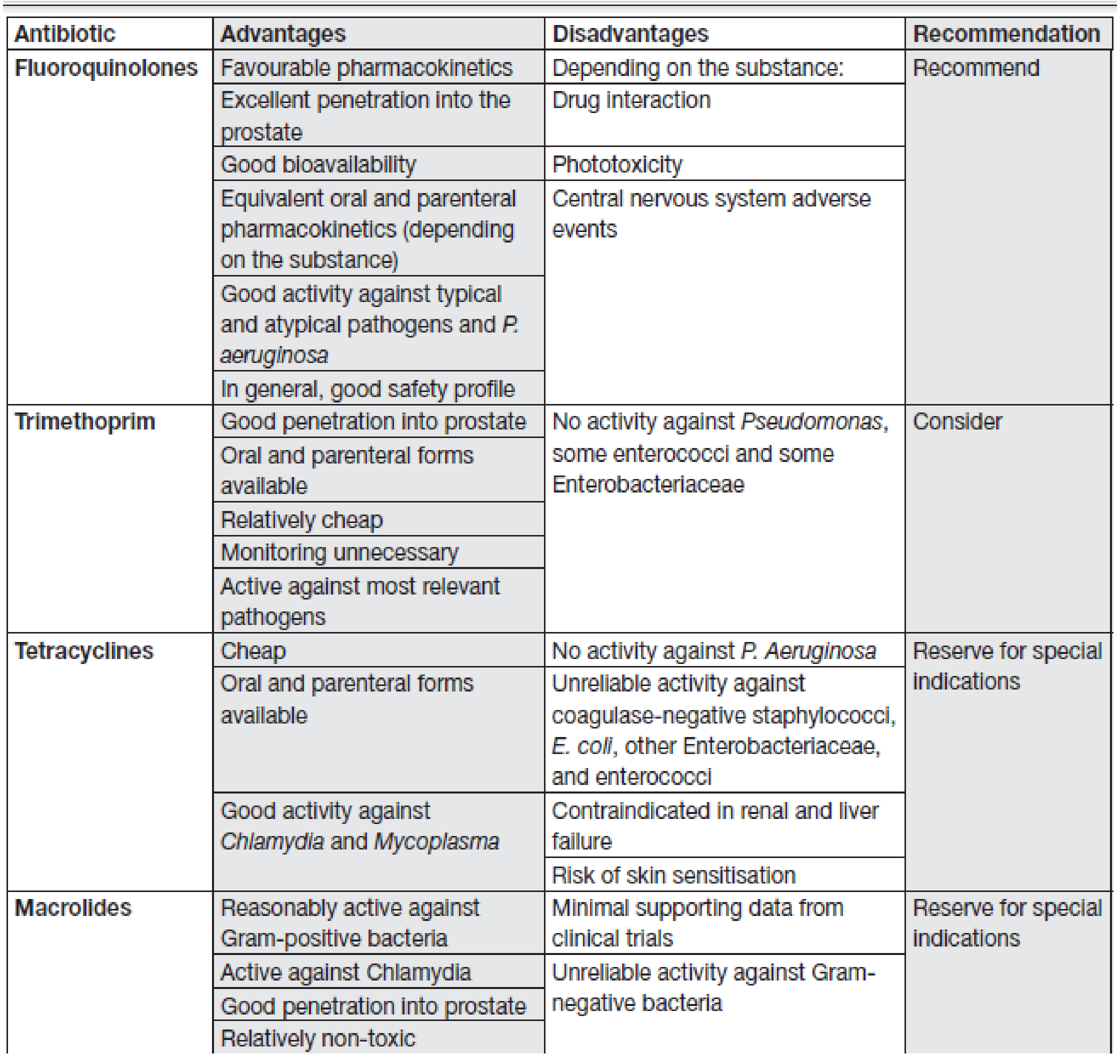
8) **A**llopurinol

- 5ARI activity, α-blocker activity, and anti-inflammatory properties

- *Serenoa repens* (saw palmetto), cernilton (bee pollen), Quercetin (flavonoid)

Table 10.5: Antibiotics in chronic bacterial prostatitis*

قراءة

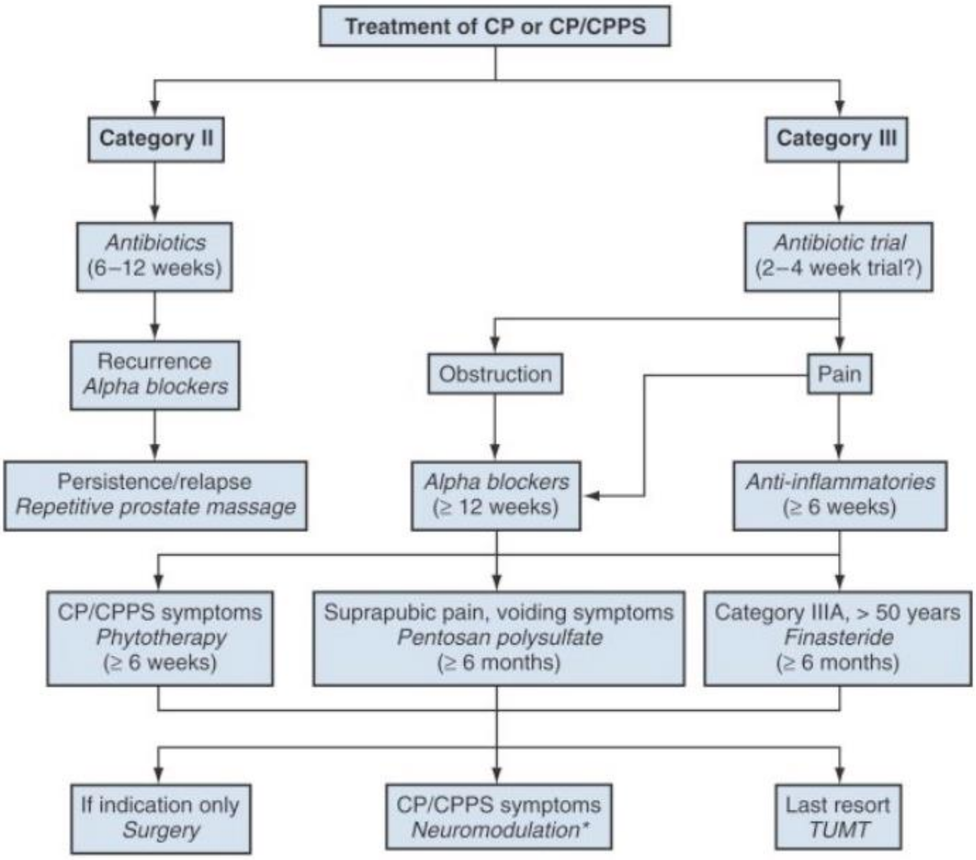


Antibiotic	Advantages	Disadvantages	Recommendation
Fluoroquinolones	Favourable pharmacokinetics Excellent penetration into the prostate Good bioavailability Equivalent oral and parenteral pharmacokinetics (depending on the substance) Good activity against typical and atypical pathogens and *P. aeruginosa* In general, good safety profile	Depending on the substance: Drug interaction Phototoxicity Central nervous system adverse events	Recommend
Trimethoprim	Good penetration into prostate Oral and parenteral forms available Relatively cheap Monitoring unnecessary Active against most relevant pathogens	No activity against *Pseudomonas*, some enterococci and some Enterobacteriaceae	Consider
Tetracyclines	Cheap Oral and parenteral forms available Good activity against *Chlamydia* and *Mycoplasma*	No activity against *P. Aeruginosa* Unreliable activity against coagulase-negative staphylococci, *E. coli*, other Enterobacteriaceae, and enterococci Contraindicated in renal and liver failure Risk of skin sensitisation	Reserve for special indications
Macrolides	Reasonably active against Gram-positive bacteria Active against Chlamydia Good penetration into prostate Relatively non-toxic	Minimal supporting data from clinical trials Unreliable activity against Gram-negative bacteria	Reserve for special indications

Which ABx's concentrate well in the prostate, and which do not?

- Good intraprostatic concentrations
  - TMP
  - fluoroquinolones
- Poor intraprostatic concentrations
  - SMX
  - ampicillin
  - carbenicillin
  - aminoglycosides

***** most Abx's get into prostate well in acute infection**


Treatment of CP or CP/CPPS
Category II
Category III
Antibiotics (6–12 weeks)
Antibiotic trial (2–4 week trial?)
Recurrence Alpha blockers
Obstruction
Pain
Persistence/relapse Repetitive prostate massage
Alpha blockers (≥ 12 weeks)
Anti-inflammatories (≥ 6 weeks)
CP/CPPS symptoms Phytotherapy (≥ 6 weeks)
Suprapubic pain, voiding symptoms Pentosan polysulfate (≥ 6 months)
Category IIIA, > 50 years Finasteride (≥ 6 months)
If indication only Surgery
CP/CPPS symptoms Neuromodulation*
Last resort TUMT

Non-Medical ttt

- acute prostatitis w/ Urinary retention→Cath.(SP, intermittent or ..).
- Prostatic abscess→drainage + conservative ttt strategies (acc. To size)

1) Surgery (better avoided in ttt of bact. Prostatitis):

- Minimally invasive Rx (balloon dilation, TUNA, TUMT (promising)
- CIC or short-term catheter (S/P tube for long term relief of BOO)
- Transurethral incision of prostatic abscess seen on TRUS or CT
- TUI of BN } if UDS evidence of BN obstruction
- TURP } for refractory category II prostatitis

2) Acupuncture (investigational)

3) Ejaculate frequently

4) Prostatic massage (historical treatment**)**

- some improvement found (frequent ejaculations same results)

5) Psychologic support (part of multi-dimensional care)

6) Biofeedback

7) Pelvic perineal Floor Massage Training + myofascial trigger point release

- eg heat therapy, physiotherapy massage, stretching, \ investigational anesthetic injections, etc.

8) Pudendal nerve entrapment therapy

Summary and recommendations

- Bacterial prostatitis is a **disease entity diagnosed clinically and by evidence of inflammation and infection localised to the prostate.**

- According to the duration of symptoms, bacterial prostatitis is described as either acute or chronic (symptoms persist > 3 months)
    - NIDDK of NIH classification distinguish bacterial prostatitis with confirmed or suspected infection from (CPPS)

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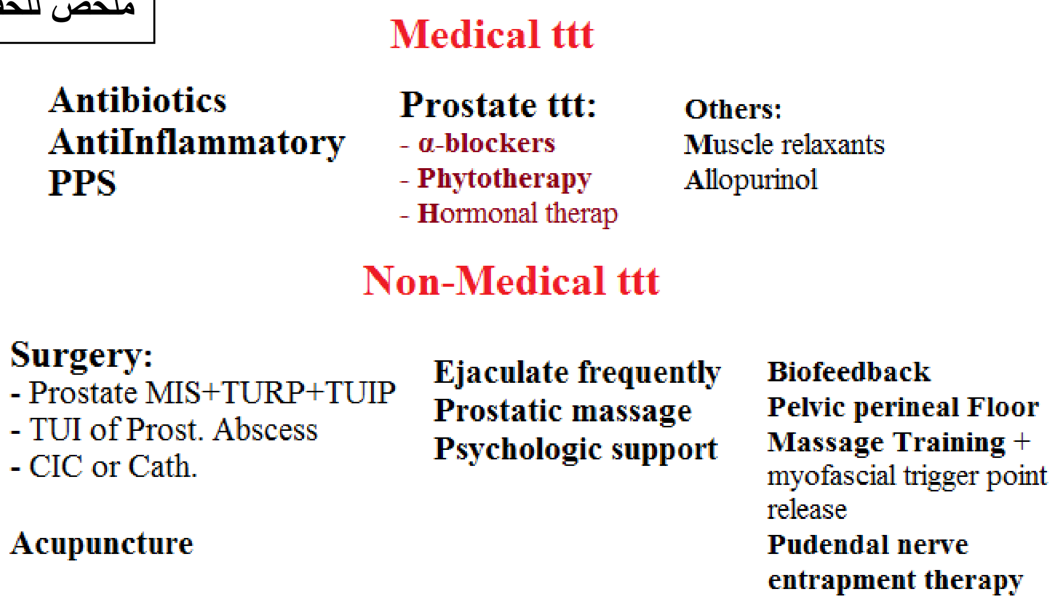

Medical ttt

Antibiotics
AntiInflammatory
PPS

Prostate ttt:
- **α-blockers**
- **Phytotherapy**
- Hormonal therap

Others:
Muscle relaxants
Allopurinol

Non-Medical ttt

Surgery:
- Prostate MIS+TURP+TUIP
- TUI of Prost. Abscess
- CIC or Cath.

Acupuncture

Ejaculate frequently
Prostatic massage
Psychologic support

Biofeedback
Pelvic perineal Floor Massage Training +
myofascial trigger point release
Pudendal nerve entrapment therapy

Epididymitis and Orchitis

- Epididymitis is almost always unilateral and relatively acute in onset.
    - The majority of cases in sexually active males aged < 35 years are due to sexually transmitted organisms.

Definition and classification

- **Epididymitis**, inflammation of the epididymis, causes pain and swelling which is almost always unilateral and acute in onset.
    - In some cases, the testes are involved in the inflammatory process (epididymoorchitis).
- **Orchitis:** inflammatory processes of the testicle, especially virally induced, often involve the epididymis.
- Orchitis and epididymitis are classified as acute or chronic processes according to the onset and clinical course.

Incidence

- Acute epididymitis in young men is associated with sexual activity.
- The most common type of orchitis, mumps orchitis, develops in 20-30% of post-pubertal patients with mumps virus infection.
    - Primary chronic orchitis is a granulomatous disease, and a rare condition with uncertain aetiology.

Causative organism

- The majority of cases of epididymitis are due to common urinary pathogens, which are also the most common cause of bacteriuria.
- Gram-negative diplococcic e.g. *N. gonorrhoeae*
- non-gonorrhoeal urethritis. *C. trachomatis*

Complications in epididymo-orchitis

- abscess formation,
- testicular infarction,
- testicular atrophy,
- development of chronic epididymal induration and
- infertility.

Pathogenesis

- Typically, in epididymitis **due to common bacteria and sexually transmitted organisms**, the infection is spread from the urethra or bladder.

Pathology

- In non-specific granulomatous orchitis, autoimmune phenomena are assumed to trigger chronic inflammation.
  - Paediatric orchitis and mumps orchitis are of haematogenous origin.
- Epididymo-orchitis is also seen in systemic infections such as tuberculosis, brucellosis and cryptococcus disease.

Diagnosis

- In acute epididymitis,
  - The inflammation and swelling begin in the tail of the epididymis and spread to testicular tissue.
  - The spermatic cord is usually tender and swollen.
  - All men with epididymitis that is caused by sexually transmitted organisms have a history of sexual exposure.
  - patient is examined immediately after urinalysis, urethritis and urethral discharge may be missed.
  - The microbial aetiology of epididymitis can usually be determined by examination of a **Gram stain of a urethral smear and/or an MSU** for the detection of Gram-negative bacteriuria.
    - The presence of intracellular Gram-negative diplococci on the smear correlates with infection with *N. gonorrhoeae*.
    - The presence of only WBC on a urethral smear indicates the presence of non-gonorrhoeal urethritis. *C. trachomatis* is isolated in approximately two thirds of these patients
  - **Ejaculate analysis** according to WHO criteria including leukocyte analysis indicates persistent inflammatory activity.
    - Azoospermia due to complete obstruction of both epididymides is a rare complication.

- If mumps orchitis is suspected, a history of parotitis and evidence of **IgM antibodies** in the serum supports the diagnosis.

Differential diagnosis

- **epididymitis and spermatic cord torsion**
    - including the age of the patient, history of urethritis, clinical evaluation and Doppler (duplex) scanning of testicular blood flow.

Treatment

- A urethral swab and MSU, before antimicrobial therapy
    - (puncture of the epididymis showed similar results).
- **Fluoroquinolones** → the drugs of first choice.
    - Fluoroquinolones (e.g. ofloxacin and levofloxacin) with activity against *C. trachomatis*.
    - favourable penetration into the tissues of the urogenital tract.
- Antimicrobials on the empirical basis:
    - in young, sexually active men → *C. trachomatis,*
    - In older men, with BPH or other micturition disturbances, the most common uropathogens are involved.
- If *C. trachomatis* has been detected as an aetiological agent,
    - treatment could also be continued with **doxycycline, 200 mg/day**, for a total period of at least 2 weeks.
    - Macrolides may be used as alternative agents.
- **Supportive therapy** includes:

  - Bed rest, up-positioning of the testes and antiphlogistic therapy (anti-inflammatory).
  - In young men, epididymitis can lead to permanent occlusion of the epididymal ducts and thus to infertility, therefore, one should consider antiphlogistic therapy with **methylprednisolone, 40 mg/day**, and reduce the dose by half every second day.

- In case of *C. trachomatis* epididymitis, the **sexual partner** should also be treated.
- Abscess-forming epididymitis or orchitis also needs surgical treatment.
- Chronic epididymitis can sometimes be the first clinical manifestation of urogenital tuberculosis.

Summary and recommendations

- Orchitis and epididymitis are classified as acute or chronic processes according to the onset and clinical course.
- The most common type of orchitis, **mumps orchitis**, develops in 20-30% of post-pubertal patients with mumps virus infection.
- If mumps orchitis is suspected, a history of parotitis and evidence of IgM antibodies in the serum supports the diagnosis.